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MENINGOCOCCAL MENINGITIS: AN-ANALYSIS OF 100 CASES*

By

FRANCIS B. JOHNSON, M. D., AND J. E. L. REVELEY, B. S., M. D., CHARLESTON, S. C.

During the winter of 1935-36 there occurred in Charleston, S. C., an outbreak of cerebrospinal meningitis in which there were 105 cases in Charleston, city and county. Five of these cases were never admitted to the Roper Hospital.

There were 100 cases admitted to the contagious department of Roper Hospital between December 12, 1935, and July 27, 1936.†

During the period in which these 100 cases of meningococcal meningitis were admitted there were nine cases pneumococcal, one streptococcal and one influenzal meningitis.

The first two cases of meningococcal meningitis occurred in the same family and were admitted in December. More than thirty days elapsed before the third case was admitted in the middle of January. During February and March 74, about three fourths of the total number of cases, developed. The number diminished during April and May and ceased the latter part of June with the exception of one admission July 27.

Eighty per cent of the cases were males and ninety-five per cent negroes, only 5 cases were found in whites. The high incidence in the negroes was probably due to the crowded living conditions associated with an unusually severe winter. There appeared to be no central focus of infection, but numerous small foci were found throughout the city and suburbs. 68 cases were from within the city limits and 42 cases from the suburbs. In 5 instances there were more than one case occurring in a single family. In one family there were 4 cases, in another 3 cases, and in three others two cases each.

In regard to the age distribution of patients 56 were under 21 years of age. 28 of this number were 12 years of age and under. Most of the cases were evenly divided between the first three decades. That is; 23 were ten years and under; 33 were 11-20 years inclusive, and 29 were 21-30 years of age. The youngest was 9 months and the oldest 45 years. It will be noted that 19, the largest group of cases, occurred between the ages 11-15 inclusive; 17, the next largest group, occurring between 21 and 25.

The most prominent symptoms noted on admission were fever, headache, pain and stiffness of the neck, nausea and vomiting, delirium, and coma in the order named. The majority of all patients were stuporous. Less frequent symptoms are noted in Table I.

The most prominent signs found were fever and positive Kernig. Petechiae were

*From Department of Clinical Pathology, Medical College of the State of S. C. and Roper Hospital.

†These cases were on the services of Dr. J. J. LaRoche and Dr. J. I. Waring. One of the writers (F. B. J.) had charge of the clinical laboratory service, and the other (J. E. L. R.) was interne part of the time on the contagious service and part of the time on the laboratory service. The bacteriological cultures were done under the direction of Dr. G. McF. Mood, and the post mortem examinations under Dr. K. M. Lynch.

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not more frequently observed because so many of the patients were negroes. In the five white patients petechiae were noted in one case. This child, aged 3 years, had a very fulminating type with onset characterized by chill, fever, and vomiting. Within 18 hours he lapsed into deep coma with Cheyne-Stokes respiration, temperature 106, imperceptible, pulse, petechiae, absence of all reflexes, simulating a generalized flaccid paralysis. Usual signs of nuchal rigidity with positive Kernig and opisthotonos were not present. He died within one hour of admission while a spinal tap was being done. Smear and culture of cerebro-spinal fluid were both positive for meningococci, and autopsy showed acute meningitis with petechiae of skin, mucous membranes, and internal organs.

TABLE I

Meningococcal Meningitis Symptoms and Signs on Admission

Headache	71	Kernig	70
Neck Pain	53	Brudzinski	8
Opisthotonous	8	Nausea or	
Chill	17	Vomiting	20
Coryza	14	Pharyngitis	9
Coma	5	Delirium	11
Stuporous	65	Convulsions	2
Abd. Pain	5	Leg Pain	3
No History	7	Rash	1
Fever	77		

TABLE II

Early White Cell Count per c. mm. of Blood in 92 Cases

Total W. B. C. Thous.	No. Cases	Total W. B. C. Thous.	No. Cases
5-10	2	20-25	28
10-15	17	25-30	5
15-20	36	30-36	4

Blood counts early in the disease in 92 cases (Table II) show that 36, or 39 per cent, had a total white count of 15,000 to 20,000 per cu. mm. 28 cases, or 30 per cent, ranged from 20,000 to 25,000, making a total of 69 per cent from 15,000 to 25,000. Only two counts were less than 10,000 and 9 above 25,000.

TABLE III

Early Per Cent of Neutrophils in Blood in 88 Cases

	No. Cases		No. Cases
70-75	8	85-90	32
76-80	11	91-95	18
81-85	16	96-97	3

A total of 88 differential blood counts (Table III) were made; of this number, 36 per cent showed a neutrophilic leucocytosis between 85 and 90 per cent, and 62 per cent between 85 and 95 per cent. 78 per cent of the differential counts were over 80 per cent. The highest count was 97 per cent neutrophils and the lowest 70 per cent.

TABLE IV

Cerebro-Spinal Fluid Cell Counts on Admission of 99 Cases

Per Cu. MM.	No. Cases
Below 500	12
500-1,000	2
1,000-5,000	37
5,000-10,000	24
10,000-20,000	20
20,000-40,000	4

Of the total cerebro-spinal fluid cell counts done on admission (Table IV) 51 were below 5,000; 24 ranged between 5,000 and 10,000; 20 between 10,000 and 20,000; and 4 were above 20,000. The highest count was approximately 40,000. The percentage of neutrophils in 81 of the cases (Table V) was between 90 per cent and 100 per cent. Nine between 75 per cent and 90 per cent and one 50 per cent neutrophils.

TABLE V

Cerebro-Spinal Fluid Cytology on Admission of 96 Cases

	No. Cases
50% Neutrophils	1
75-85% Neutrophils	5
85-90% Neutrophils	4
90-95% Neutrophils	32
95-100% Neutrophils	49
95-100% Lymphocytes	6

Some very interesting findings were observed on those cases with low cerebro-spinal fluid cell counts on admission. 12 cases had counts

below 317. 8 of these 12 cases had counts below 17. Of these, 6 showed a predominance of lymphocytes. One of these cases with early negative findings that later developed typical meningitis will be dicussed.

Case No. 85239, M. E. J., a four year old colored female, was admitted 2-11-36 with history of fever, sore throat, nausea, and vomiting of three days duration. Physical examination showed temperature 103, pulse 104, respiration 36, purulent nasal discharge, enlarged inflamed tonsils, and pharynitis. All neurological signs were negative. Spinal tap showed clear fluid, normal in every way. The patient was transferred to the observation ward. Next morning, Feb. 12, 1936, her temperature had dropped to 99.4 but it rose in the afternoon to 104.3. A second tap showed bloody fluid with no increased pressure. Her total white blood count was 22,650 with 73 per cent neutrophils. She appeared drowsy, but her temperature became sub-normal on the 13th and remained low until the morning of the 14th. At this time she developed a positive Kernig, and the third tap showed bloody fluid under increased pressure. Therefore she was given 15 c. c. anti-serum intra-spinally and 15 c. c. intra-muscularly and 10,000 units anti-toxin intra-muscularly. The following day, Feb. 15th, cloudy fluid was obtained by cisternal puncture with a cell count of 1,126, neutrophils 89 per cent, negative smear and culture. On Feb. 16th, in view of a normal temperature, a cell count down to 369 and a negative culture, no further serum was given. From the 16th to the 23rd the cerebro-spinal fluid was clear with negative cultures, and she remained afebrile and apparently improving. A tap on the 23rd showed a cell count of 135, with a positive culture. She was promptly transferred to the contagious ward, serum-therapy instituted, and the patient finally recovered.

TABLE VI

Meningococcus in Cerebro-Spinal Fluid on First Examination

Smear Positive	74 %
Culture Positive	76 %
Smear & Culture Positive	62.5%
Smear & Culture Negative	11.5%
Neg. Smear—Pos. Culture	15.3%
Pos. Smear—Neg. Culture	10.6%
No Smear recorded	5 cases
No Cultures recorded	11 cases

Of 95 early smears of cerebro-spinal fluid (Table VI) 74 per cent were positive and 26 per cent negative. Of 89 early cultures 76 per cent were positive and 24 per cent negative. There were 85 cases in which both smears and cultures were made. 62 per cent of these agreed positive; 11.5 per cent agreed negative; 15.3 per cent had negative smears and positive cultures; 10.6 per cent had positive smears and negative cultures. Numerous smears and cultures were made in addition to the above mentioned early examination.

Nine cases of the series had negative smears and negative cultures throughout the course of their disease. All of these had elevated spinal fluid cell counts with fluid under increased pressure, elevated blood leucocyte counts, and had definite symptoms and signs of meningitis. Two were confirmed at autopsy, and the remaining seven recovered after serum therapy.

The strain of meningococcus found belonged chiefly to type three, though some types one and two were found, as reported by Dr. G. McF. Mood, and have, strangely enough, produced primary cultural growth on liquid media of dextrose and two c. c. of human blood serum more satisfactorily than on solid media of human serum and agar. Best cultural results for maintenance were, however, obtained on a media of human blood serum and agar.

From our general observation of the laboratory findings in this series of cases there was a lack of correlation between the total cerebro-spinal fluid cell count and the presence or absence of organisms detected by smear or culture before treatment. Contrary to the usual text book teachings, we found cases in which the count was 5,000 or over with negative smears or cultures and other cases in which the count was below 1,000 with positive smears or cultures.

Case No. 86560, F. B., is worthy of detailed discussion: This 32 year old colored female was admitted with history of rapid onset of headache, fever, generalized aching, and chills 24 hours previously. She had vomited once and had been perfectly well until that time.

Physical examination revealed temperature 100.8, pulse 96, respiration 24; positive physical signs of stupor, sluggishly reacting pupils, congestion and reddening of nasal mucosa, moderate nuchal rigidity with positive Kernig, and hyperactive knee jerks. Spinal tap showed slightly cloudy fluid under moderately increased pressure. The count was 225 with neutrophils predominating and both smear and culture positive for meningococci. She was given 30 c. c. of anti-serum intra-spinally and 30 c. c. intra-muscularly immediately after the first tap. The next day the cerebro-spinal fluid count was 3,800 with positive smear and the total white blood count was 22,150 with 84 per cent neutrophils. Within one week after daily taps and serum by spinal and muscular routes her culture and smears were negative, her temperature down, and patient symptom free. Discharged recovered 18 days after admission.

The fact that both smear and culture were positive with a total of only 225 cells in cerebro-spinal fluid is certainly interesting. This is particularly true when no organisms were seen in other cases having cell counts well above 5,000.

In our opinion, the failure to find a high count, or the presence of organisms in either high or low counts, after a single tap should by no means exclude the possibility of epidemic cerebro-spinal meningitis. In the presence of clinical symptoms the patient should be carefully isolated until further taps or other diagnostic procedures have been carried out.

We will cite a particularly striking case: Case No. 85445, N. G., who was admitted with very few physical signs and symptoms except for temperature 103 and headache. Spinal fluid showed a cell count of 11 c. mm., with 86 per cent lymphocytes. Nine and one-half hours later his temperature had risen to 107.6 by rectum and a tap 17 hours from the first tap showed the phenomenal rise to a cell count of 8, 634. with 98 per cent neutrophils and many organisms in the direct smear.

Another patient, J. C., No. 85655, had a rise in 17 hours from 3 lymphocytes to 2,176 with neutrophils greatly predominating. Early serum-therapy was instituted because of increased pressure, and positive smear or culture was not obtained.

The usual plan of treatment was a daily spinal tap followed by anti-serum intra-spinally and intra-muscularly. A few cases were also given anti-serum intra-venously. In general, two-thirds of the total amount of anti-serum was given by the intra-muscular route in each case. The average daily dose of anti-serum was 45-60 c. c.

TABLE VII

Anti-serum Treatment	Cases
Total Recovered	81
Less than 300 c. c.	32
From 300-500 c. c.	32
Over 500 c. c.	17
Serum and Antitoxin	14
10,000 units or less	4
20,000-80,000 units	4
More than 150,000 units	2

Of the 81 patients that recovered, 32 received less than 300 c. c., 32 from 300 to 500 c. c. and 17 more than 500 c. c. The least amount given with recovery was 120 c. c. and the largest 910 c. c. in a case that relapsed.

Active anti-serum treatment was continued until the cerebro-spinal fluid count approached normal; the smears and cultures negative and the patient free of symptoms.

Fourteen cases that recovered were given both anti-serum and antitoxin. However, seven of these received only 10,000 units because the antitoxin was difficult to obtain. Five received from 10,000 to 80,000 units. Only two received more than 150,000 units and no case was treated with antitoxin alone.

TABLE VIII

Days of Anti-Serum Treatment in 81 Cases With Recovery

	Cases
4-12 days	71%
12-37 days	21%
17-26 days (relapses)	8%

In 71 per cent of 81 cases that recovered (Table VIII) active anti-serum treatment was carried out over a period of four to twelve days. 21 per cent were treated from twelve to thirty-seven days. 8 per cent consisted of 6 cases which relapsed and therefore received treatment totaling 17 to 26 days.

We would like to emphasize that the fore-

going figures referring to treatment include only the 81 cases which recovered.

TABLE IX
Morbidity

Hospital Days	No. Cases
10 to 12	4
12 to 15	9
15 to 18	13
18 to 20	12
21 to 25	13
25 to 30	12
30 to 35	5
35 to 71	12

The morbidity (Table IX) in 64 cases, or 80 per cent, was 10 to 30 days hospitalization. The average stay in hospital of 81 recovered cases was 25 days. One case spent 71 days in the hospital and had three relapses with final recovery. Another case was discharged after 8 days as recovered and returned 2 months later with a relapse, or recurrence, remaining 24 more days.

Case No. 84328, D. R. This 14 year old colored male was admitted with history of malaise, headache for three days, with muscular rigidity, delirium, and increasing opisthotonos one day before admission. Physical examination revealed temperature 101, respiration 30, pulse 104; small fixed pupils; marked nuchal rigidity with opisthotonos and spasticity of legs. Cerebro-spinal fluid was very thick and purulent with cell count 40,000, 90 per cent neutrophils and positive on direct smear and culture. Over the 11 day period between Dec. 11, 1935, and Dec. 22, 1935, he was given 305 c. c. of anti-serum and 20,000 units antitoxin. Within this period his temperature became normal and his cerebro-spinal fluid count 137 with negative culture. Serum was omitted and patient continued to improve and was afebrile from Dec. 23, 1935, to Jan. 8, 1936. The morning of Jan. 8 he complained of headache, his fever rose within 6 hours to 103, and a tap showed a cerebro-spinal fluid count of 3,898, neutrophis 97 per cent with direct smear positive. Serum therapy was resumed, and within 6 days on Jan. 14 cell count was 49 with negative culture and temperature normal. On the 18th he had a third rise of temperature and another rise in cerebro-spinal fluid count to 4,053 with neutrophils 95 per cent, although serum therapy had not been discontinued, and culture was negative. His temperature returned to normal and cerebro-spinal fluid cell count again dropped to 87 by Jan. 22 and anti-serum was again omitted. A total of 420 c. c. of anti-serum and 25,000 units of antitoxin was given during this second two weeks period from Jan. 8 to Jan. 22.

On Jan. 29 he had a fourth rise in temperature, but cerebro-spinal fluid culture was negative. 30 c. c. of serum was given on Jan. 30th, and patient had a slight reaction. Serum was withheld, the patient ran a septic temperature for 4 days and became afebrile for 2 days on Feb. 3 and 4. He again ran a septic temperature from Feb. 5 to 9. Repeated smears for malaria were negative and cerebro-spinal fluid culture negative. Fluids were forced and patient was discharged recovered on Feb. 21 after 12 afebrile days. He spent a total of 82 days hospitalized and was given 755 c.c. of anti-serum and 45,000 units antitoxin, having had three relapses in that time.

TABLE X
Meningococcal Meningitis Mortality Rate in 100 Cases Treated with Antimeningococcal Anti-Serum

Total deaths	19%
Excluding 6 within 7 hours	13%
Excluding 8 within 24 hours	11%
Excluding 10 within 36 hours	9%
Excluding 11 within 48 hours	8%
Excluding one case anaphylaxis in hospital 76 hours	7%

There were 19 deaths (Table X) out of 100 cases admitted to the hospital. 12 autopsies were performed. On closer analysis 6 of these deaths occurred within 7 hours of admission, reducing the mortality to 13 per cent; two additional deaths within 12-24 hours brings the mortality rate down to 11 per cent; two between 24-36 hours, still further reduces the mortality rate to 9 per cent, and one death after 36 hours makes a total of 11 dying within 48 hours after admission. Therefore only 8 deaths occurred with patients in the hospital more than 48 hours. One of these had been in the hospital 76 hours and died of anaphylaxis after 60 c. c. of anti-serum. Therefore, the

mortality in cases treated in the hospital more than 48 hours was 8 per cent; excluding this case of anaphylaxis the mortality was 7 per cent.

Of the 6 cases that died within 7 hours, 3 were comatose and moribund on admission, with imperceptible pulse and Cheyne-Stokes respiration; two were not moribund but died after serum therapy from anaphylactic shock, which was proven at autopsy. The sixth case died within 7 hours after admission and 5 hours after serum therapy with no evidence of anaphylaxis. No autopsy was obtained in this case. In two cases dying 14 and 24 hours respectively, the first was comatose and the second irrational on admission; and neither responded to treatment. The remaining three cases were in the hospital 25, 31, and 38 hours respectively and failed to respond to treatment. One of these showed a complicating pneumonia at post mortem; another broncho-pneumonia and acute internal hydrocephalus; the third a two months pregnancy.

Of the 8 cases dying that were hospitalized more than 48 hours, 4 showed an internal hydrocephalus at autopsy, and a fifth, in which no autopsy was obtained, also showed clinical evidence of block. One of the cases dying from internal hydrocephalus was of special interest.

Case No. 85478, C. W. This 18 year old boy gave a history of illness 6 days before admission. He was given 315 c. c. of anti-serum in 5 days; he became afebrile the last nine days and was discharged 16 days after admission with a cerebrospinal fluid cell count of 111 with negative culture. 7 days after discharge he was readmitted with history of recurrence of headache and fever 4 days previously. Spinal fluid count was 23,000 with positive smear and culture. He was given 320 c. c. of anti-serum in the next 10 days and became afebrile for the following 14 days with general improvement and cerebro-spinal fluid cell count 340 with negative culture. On the following day his temperature went up to 103 with recurrence of headache and stiff neck; cerebro-spinal fluid cell count 2,100 and positive smear and culture. He was given 90 c. c. of anti-serum and died the next day. Autopsy showed acute purulent meningitis with internal hydrocephalus.

Therefore, 5 of the 8 cases dying after 48 hours were complicated by internal hydrocephalus with block. The sixth case died of anaphylaxis as previously stated.

The remaining two cases died after 3 and 4½ days hospitalization, respectively; did not appear unusually ill on admission, but failed to respond to treatment. No autopsies were obtained on these two.

The percentage of deaths was approximately the same in both children and adults.

Of 87 cases in which a definite history of onset of illness was obtained, 59 had been ill three days or less before admission, and of these 12 per cent died (excluding anaphylaxis). In the remaining 28 cases which had been ill four to eight days inclusive, 25 per cent died (excluding 2 anaphylactic deaths). It can be concluded in this series of cases that early anti-serum therapy within three days of onset of symptoms was a factor influencing the low mortality.

Contrary to the method of treatment in which early massive doses of anti-serum or antitoxin was given and infrequent spinal punctures used only for relief of pressure symptoms, this series responded well to frequent spinal taps and frequent small doses of serum for a period of days as previously given in Table VIII. Not only was the mortality lower, but the morbidity compared favorably, with a series of cases reported by Hoyne* who had a mortality rate of 9.6 per cent in 85 cases treated with antitoxin and mortality rate of 29.6 per cent in 211 anti-serum treated cases excluding deaths within 48 hours, while our series had a mortality rate of 8 per cent, excluding deaths within forty-eight hours.

SUMMARY

1. An analsysis of an outbreak of 100 cases of meningococcal meningitis occurring in Charleston, S. C., and suburbs is presented. These cases were scattered over a considerable area with no central focus of infection. 95 per cent were in the colored race; 80 per cent were in males; and only 28 per cent in children.

2. Twelve of the cases had, on the first spinal tap, below 317 cells per c. m. in the cerebro-spinal fluid. Eight of these had counts below 17, and of these, six showed a predominance of lymphocytes on the first examination.

*Hoyne, Archibald L. Jour. A. M. A. 104: 980-983, March 23, '35.

3. In the examination of the cerebro-spinal fluid, there was a lack of correlation between the total cell count and the presence or absence of meningococci. In some cases counts below 500 cells per c. mm. showed meningococci, while other counts above 5,000 per c. mm. failed to show positive smears or cultures.

4. The failure to find, on early examination, a high cerebro-spinal fluid cell count, or to find meningococci in either high or low counts, after early spinal taps should by no means exclude the possibility of meningococcal meningitis.

5. Frequent spinal taps with the use of repeated doses, chiefly intra-muscularly and intra-spinally, of anti-meningococcal serum was the method of treatment in this series of cases.

6. The death rate was 19 per cent, including all deaths. Excluding those dying within forty-eight hours, the death rate was 8 per cent.

DISCUSSION

Dr. G. McF. Mood, Charleston:

Dr. Johnson has presented a very exact and comprehensive report of the recent outbreak of epidemic meningitis occurring in Charleston. There are several interesting points occurring in this epidemic to which he has alluded, one being the fact that a tremendous majority occurred in the negro population. I am not at all sure that the explanation that this was due to overcrowding is a satisfactory one. While it may be true that just at that time there was an unusual overcrowding among some of the negro population due to condemnation of numerous negro tenement houses, there was apparently no equivalent condition existing outside of the city and the report shows almost 50% of the cases occurred in the county outside of the city.

When I recall the outbreak of 1916-1917, few negroes were attacked, the majority of cases being confined to the white population, and at that time the negro population as well as the white population of Charleston had tremendously increased, there being between 25,000 and 30,000 more people in Charleston than the census has shown since that date. There probably was as much overcrowding at that time as existed in the recent outbreak. I do not believe that a satisfactory explanation can be offered at this time for the occurrence of the cases almost entirely among the negro race. Possibly the strain of organisms has something to do with it. Another unusual feature, purely a laboratory one, is the fact that these organisms were grown with great difficulty, and frequently not at all, on solid media when primary cultures were made from spinal fluids. Most meningococci grow rather poorly on liquid media, better on solid media. Almost without exception, these strains encountered at this time grew much more luxuriantly on liquid media. After primary cultures were obtained upon liquid media, the organisms grew very well upon any of the various recommended solid media.

The most important consideration of epidemic meningitis today is the public health side. For many years we have been more or less content with culturing the naso-pharynges of contacts, isolating those carrying meningococci. When one looks over the literature of these years he can not but be impressed with the fact that such segregations have apparently accomplished nothing. This is due to the fact that most of the strains cultured along with other bacteria from the naso-pharynx and grown easily and readily upon any of the recommended culture media are either saprophytic strains or strains of so slight virulency that they may be aptly classed as occasionally parasitic and accountable probably for the occurrence of a sporadic case or so. The true parasitic and epidemic strain is interfered with by the growth of other organisms from the pharynx and is grown with more difficulty and apparently is less frequently found. Adhering to the grouping suggested by Gordon of four types of meningococci, it has been shown by Rake that types 1 and 3 are parasitic strains and that 2 is occasionally parasitic only and 4 a harmless saprophyte. In order to be certain that one has found a carrier which means anything at all in the control of an epidemic of this disease it is necessary that the culture obtained from the carrier be typed and proven to belong to a parasitic group, i. e., 1 or 3. These may be spoken of as key strains. When such are found and the carrier isolated, one may feel that he has accomplished something. Unless these are found, the indiscriminate culturing of all contacts continues to be a useless procedure. Laybourne, writing in the *American Journal of Public Health*, October, 1936, puts the whole problem very clearly as follows: "Outbreaks of meningococcus meningitis offer adequate evidence of the futility of the control measures which have been employed, and the literature gives slight promise of the immediate development of effective control measures which can be generally applied. Carriers have commonly been considered more important in the transmission of the disease than cases, yet carrier surveys, as usually carried out, have complicated the administrative problems involved without aiding materially in control. The carrier incidence in a group may run above 35 per cent and the outbreak abate without their segregation. In other instances, the segregation of carriers, as found, has had no influence on the course of the outbreak. As a result of such observations the wholesale meningococcus carrier survey has fallen into disrepute, probably to the best interests of all concerned.

"The wholesale carrier survey has, however, at least, served to emphasize the fact that there are many problems in the bacteriology, infection, immunity, and epidemiology of meningococcus meningitis which have not been worked out or have been ignored in routine work." One must remember, too, that meningitis falls among the group of limited suscepti-

bility. If skin tests with meningococcus toxin are accepted as an accurate indication of susceptibility, Laybourne has shown that out of a group of 626 people exposed to meningitis during epidemics, only 1.5 per cent were highly susceptible, 25.7 per cent were slightly susceptible and the remaining 72.8 per cent showed no susceptibility. Due to this limited susceptibility and the infrequency of effective meningococcus carriers, outbreaks have been known to decline rapidly without any segregation when the carrier incidence in a group runs as high as 35 per cent.

One of the encouraging findings within recent years is the production of meningococcus toxin by Ferry, Norton, and Steele which offers the hope and possibility that within a few years this product may be used, on the one hand, for the making of skin tests for the determination of susceptibility, and on the other for the active immunization of those found susceptible. Important work has been done on this latter phase by Kuhns and Laybourne.

I have enjoyed listening to and discussing Dr. Johnson's interesting paper.

Dr. J. J. LaRoche, Charleston:

In reference to the paper of Dr. Johnson on the epidemic form of cerebro-spinal meningitis, which has been so ably presented, there is little I can add except to say a few words regarding the very early symptoms, the diagnosis, and the treatment inaugurated.

To me, in the early cases—the cases that we saw early, the following were the predominating symptoms: First, a mild nasopharyngitis—just a head cold; a moderate degre of photophobia; numbness and soreness of the muscles of the neck and of other muscles, at times. The chin, however, could be brought down upon the sternum voluntarily in most cases. A negative or, at the most, a suspicious Kernig's sign, accompanied, as a rule, with a moderately elevated temperature. The one outstanding finding that I observed in every individual was the headache that she or he complained of, apparently of the most excruciating character, and without remission—a purely subjective symptom.

In the cases not observed so early the symptomatology was more or less of the text-book character.

Regarding the treatment, I was unable to determine the relative values of serum and antitoxin therapy, being forced to use, from day to day, whatever treatment was available. In my experience, however, there are three indications to be met: first, an early diagnosis; second, hospitalization; third, serum—intravenously at least once, then intramuscularly or intraspinally from day to day as the symptoms are alleviated. But, above all, spinal puncture should be done at least once a day for several days after tthe cell count has become normal and the symptomatology is normal. The remainder of the treatment, of course, was routine.

To me the remarkable feature of this epidemic was that there were no sequelae. In the vast majority of cases the patients, when they got well, got well all over. They were not left blind; they were not left paralyzed. When they got well they got entirely well.

I want to say in conclusion, gentlemen, that the only reason we got any results, or the results that we did get at Roper Hospital, was due to the loyalty of our internes and nurses. We had to fight to keep them off the wards. They would stay in there for from fifteen to eighteen hours a day. We had to fight to get them out so they would rest.

X-RAY FINDINGS IN PEPTIC ULCER

By

CARROLL BROWN, M. D., WALTERBORO, S. C.

Peptic ulcers occur almost anywhere in the digestive tract—esophagus, stomach, duodenum, Meckel's diverticulum, caecum—but peptic ulcers other than gastric and duodenal are rare and are not considered in this discussion.

The diagnosis of peptic ulcers is largely dependent upon the X-ray examination. Barclay states that the report of a competent radiologist is regarded as of more value than all the traditional signs and chemical tests put together. However, this does not mean that the case should not be thoroughly worked out along other lines also. The X-ray findings are merely supplementary and should be carefully considered along with the history, physical findings, and other laboratory tests in a particular case before arriving at any definite conclusion. The history is especially important in the differential diagnosis of doubtful stomach lesions. In some filling defects in the prepyloric region it is often impossible to tell from the X-ray findings whether the lesion is an ulcer or an early malignancy. If the patient is young and the symptoms of relatively long duration, the chances are that it is an ulcer, if the symptoms are of short duration and the patient older, it is more likely to be malignant. Add to this the chemical analysis of the stomach contents, observe the effect of a strict ulcer diet during frequent X-ray examinations, and a fairly accurate diagnosis can be made.

The indications for an X-ray examination of the stomach are well known. However, there are some conditions in which the exami-

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nation cannot be made even though we are fairly certain that some unknown pathology is present. The contra-indications are:

1. Severe nausea and vomiting. The visualization of the stomach and duodenum depends entirely on the ability of the patient to take and retain a barium mixture. Therefore, when the patient is nauseated and vomiting, it is necessary to wait until the vomiting subsides before making the examination. This can sometimes be speeded up by "decompression of the stomach" when it is due to a large dilated stomach which is obstructed at the pylorus. The stomach is emptied with a tube and washed out several times a day, and soon regains its normal tone and size; at the same time the vomiting subsides also.

2. Extreme weakness. Obviously, if the patient is too weak to co-operate or to be handled, the examination should not be made.

3. Hemorrhage. A patient should not be X-rayed for two weeks after a hemorrhage from the gastro-intestinal tract. The stretching of the stomach walls with the barium mixture and the palpation of the stomach necessary to make a satisfactory examination is apt to start the hemorrhage again. It is a peculiar fact that when these patients do come for an examination two weeks after a hemorrhage, very often no pathology can be found—a hemorrhage seems to speed up the healing process in an ulcer.

4. Perforation. Of course if there are symptoms of acute perforation of an ulcer, barium should not be given; it is dangerous and unnecessary. Perforation liberates air into the peritoneal cavity. With the patient upright this air collects beneath the diaphragm and can easily be demonstrated between the liver and diaphragm. This sign is pathognomonic of perforated ulcer in the presence of suggestive symptoms. If it is not seen, however, it does not mean that perforation has not occurred.

5. Obstruction. When there are symptoms of acute intestinal obstruction, it is considered dangerous to give barium. This sometimes will make complete a partial obstruction.

The preparation of the patient is simple: no cathartic or anodyne 48 hours before and no breakfast on the morning of the examination.

For roentgenologic purposes the stomach may be considered anatomically in three parts: the fundus, the media, and the antrum. The fundus is that part above the level of the cardiac orifice. The body, or media, passes downward along the left margin of the spine to the line where the stomach turns across the vertebral column. The antrum is the portion from this turn to the pylorus. The position and relations of these parts vary with the position of the patient, and with different people. The prepyloric region is that portion of the antrum 1 inch proximal to the pylorus.

Gastric ulcers are outnumbered by duodenal ulcers in a ration of 6 to 1. They usually occur along the lesser curvature, occasionally on the anterior or posterior walls, and very rarely on the greater curvature. Ulcers on the anterior or posterior walls or in the fundus are sometimes very hard to demonstrate. Lesions on the greater curvature or in the prepyloric region should be considered malignant until proved otherwise. Ulcers occur anywhere from the cardiac orifice to the pylorus and vary much in size and depth. They are classified according to their depth as (1) Mucus ulcers, or very shallow erosions in the mucus membrane, and these, naturally, being so shallow are often overlooked. (2) Penetrating ulcers, which extend into the muscularis and (3) Perforating ulcers, which have extended through the serous or peritoneal coat. As a rule, malignant ulcers are shallow and benign ulcers sharply punched out and deep. If there is any doubt as to whether the lesion is malignant or not, the patient is put on a Sippy diet and examined again in about three weeks. If the lesion is benign, it will have decreased in size and there will be other evidence of healing. If there is no healing, the patient should have an exploratory operation. It has been repeatedly shown that this is the most practical method of differentiating benign and malignant gastric lesions. To show how difficult it is to differentiate these lesions by X-ray alone, I quote the following from Beckman's Treatment: "Unfortunately, there seems to be no reliable criteria by which malignancy can be determined in a given case until the tissue is subjected to microscopical examination; in 200 proved benign cases at the Mayo Clinic, suspicion of malignancy had arisen in the minds

of clinician, roentgenologist, or surgeon in 34 per cent of instances, and even with the lesion exposed the surgeon diagnosed a carcinomatous ulcer in 12 per cent of the cases."

The only possible direct evidence of a gastric ulcer is the demonstration of the nitch shadow or barium-filled crater extending beyond the shadow of the stomach. Other evidence of gastric ulcer is hour-glass stomach, obstruction, retention of barium after 5 or 6 hours, and evidence of infiltration of the stomach wall as evidenced by interference with the peristaltic waves. The patient should be examined in all positions and from all possible angles, as some ulcers are very difficult to demonstrate.

Duodenal ulcers are similar to gastric ulcers. They occur much more frequently and are, as a whole, much smaller than gastric ulcers. They appear more often on the lesser curvature of the duodenum and are usually found just beyond the pylorus in the first portion of the duodenum. They may occur right in the pylorus itself. The diagnosis by X-ray is based on the persistent deformity of the shadow of the bulb or cap, which is the first portion of the duodenum. This deformity of the bulb is sometimes due to the crater of the ulcer showing on the film, but in the majority of cases it is due to associated spasm of the musculature or exaggeration of the mucosal folds.

The crater of an ulcer is much more difficult to demonstrate in the duodenum than in the stomach and is more easily visualized in early than late cases. The most frequent finding, and the one depended on mainly in making a diagnosis, is the persistent deformity of the bulb as seen under the fluoroscope and on several films. One film is of no value in the examination of the duodenum, because the cap may be exposed on the film during contraction, and deformity may be identical with the deformity caused by an ulcer. There may be tenderness on palpation over the duodenal bulb, but the absence of tenderness is no evidence against ulcer. Peristalsis of the stomach is apt to be overactive and the emptying time shortened; but if there is much induration, a partial obstruction may be produced and cause a dilatation of the stomach with a retention of the barium meal. The accessory findings are not constant and may be produced by some condition outside the stomach or duodenum, such as gall-bladder disease or appendicitis. So in the end, for a diagnosis of duodenal ulcer we depend mainly on the persistent deformity of the bulb and a demonstration of the crater of the ulcer when possible.

Healing cannot be checked as closely as it can in a gastric ulcer. Usually the only change noted is a slight diminution in muscle spasm and disappearence of tenderness. Deformity usually persists although clinical results are satisfactory.

Malignancy occurs so rarely in the first portion of the duodenum that its differentiation from ulcer need not be considered.

As stated in the beginning, the X-ray findings in these cases are undoubtedly of great value in making a diagnosis, but they have their limitations. All ulcers are not found, and occasionally an ulcer is seen on the film when it does not exist in the patient. The safest procedure is to take a careful history, a good physicial examination, laboratory tests, and X-ray findings; if necessary, observe the patient over a period of several weeks during treatment. Carefully consider all of the information gathered, and make the diagnosis. Even then we won't always be right.

A SUMMARY OF A WASSERMANN AND KAHN TESTING SURVEY AT THE SOUTH CAROLINA PENITENTIARY

By

SEDGWICK SIMONS, M. D., ASST. EPIDEMIOLOGIST IN CHARGE OF SYPHILIS CONTROL, STATE BOARD OF HEALTH, COLUMBIA, S. C.

During the early months of the calendar year 1937 a blood-testing survey was carried out at the South Carolina Penitentiary. This study had as its cardinal purpose a serological determination of the incidence of syphilis among inmates of the Institution. Originally it was intended to include routine analyses of spinal fluids in the diagnostic procedure, but, for various reasons, it was unfortunately deemed necessary to abandon the latter consideration as totally impracticable, under circumstances existing within the Prison at the time.

Originally suggested by Dr. J. McMahon Davis, the idea of this study was warmly espous-

ed by Dr. James A. Hayne, State Health Officer, who arranged through Federal sources for the provision of necessary funds with which to carry on the work. Testing was limited to prisoners and the collection of blood samples (by syringe method) was effected under the immediate supervision of Dr. Davis and Dr. J. E. Boone, of Columbia, with the able and cheerful cooperation of Dr. L. H. Jennings, Prison Physician. All samples were tested in the Hygienic Laboratory of the State Board of Health by the Wassermann and Kahn tests. For the evaluation of data derived, the preparation of all record forms, together with the entire statistical treatment of reported facts and figures, was made by this office.

Proceeding with a highly abbreviated resume of the situation determined, it is to be noted that the entire prison population consisted of 1286 persons, of whom there were 544 whites (528 males and 16 females) and 742 negroes (679 males and 63 females). Of this group the total number tested included 1164 persons —507 whites (491 males and 16 females) and 657 negroes (599 males and 58 females)— the racial percentage proportion thus being 43.56 to 56.44, relatively commensurate figures. However, the total percentage of females (6.36) is almost too small to warrant any detailed intersexual consideration. The number of instances in which no records of tests were made were numerous—36 for whites and 84 for negroes—thus creating a test defiicit of 120, or 9.33 per cent. Under the circumstances, there arises the question as to whether or not serological results as reported would have been appreciably altered had this deficit not occurred. Percentage positivity as determined was: 8.09 for whites, 36.53 for negroes, and an average of 24.14 for both races. Percentage negativity was 91.12 for whites, 61.34 for negroes, and 74.31 for both races. The percentages of tests indicated as "doubtful" were: 0.79 for whites, 2.13 for negroes, and 1.55 for both races. In but three instances were bloods collected in amounts insufficient for examination, and it is extremely interesting to note that in not a singie instance was a specimen lost or injured in transit twixt case and laboratory, that no specimens were haemolized, and that not a single anti-complementary Wassermann occurred.

Reactions, by race and age groups appeared to follow the general trend, with the greatest percentage of positives falling in group 20-29 in both races, and the heavily preponderating percentage positivity below age 40, as may be seen by the following tables:

As to the question of serological behavior in relation to marital status, it can very definitely be stated that the percentage of married persons positive is considerably greater than that of single persons, and especially so in the white race. The percentage of positive widowed persons is disproportionately small, but the total muster of individuals in this group is too insignificant to warrant comparison. Again, as there was but one divorced person in the entire population tested, this group, also, cannot be considered.

From an occupational standpoint, and for varied purposes of expedition, the tested population has been classified under ten liberal headings. By each of these headings the occupation-specific percentage positivity was calculated, as follows: professionals, 0; clericals, 13.05; salesmen, 11.11; farmers, 14.22; food-handlers, 39.24; skilled laborers, 17.83; un-

TOTAL RACE AND SEX-SPECIFIC PERCENTAGE POSITIVITY

	WHITE			COLORED			BOTH RACES		
Age Group	Male	Female	Total	Male	Female	Total	Male	Female	Total
15 - 19	2.56	0.00	2.44	5.42	18.92	7.50	4.96	18.00	6.76
20 - 29	41.03	50.00	41.46	62.07	59.46	61.67	58.68	58.97	58.72
30 - 39	38.46	50.00	39.02	22.17	16.22	21.25	24.79	17.95	23.84
40 - 49	10.26	0.00	9.76	6.40	2.70	5.83	7.02	2.56	6.41
50 - 59	7.69	0.00	7.32	2.46	2.70	2.50	3.31	2.56	3.20
60 & Over	0.00	0.00	0.00	1.48	0.00	1.25	1.24	0.00	1.07
Total Percentage Positivity									
20 - 40	79.49	100	80.48	84.24	75.68	83.92	83.47	76.92	82.56

skilled laborers, 27.89; textile workers, 7.83; barbers and beauty parlor operators, 31.25; miscellaneous, 39.84. It is to be observed that farmers, laborers, and textile workers, taken together, comprise 77.8 per cent of the entire number tested, and that their composite percentage positivity was 67.41,—whites being represented in the percentage of 68.29 and negroes, 67.50.

Grouped according to home address, it is interesting to note that none of the prisoners reported normal residence out of South Carolina; hence, they are listed by county. In general, it may be seen that the distribution is more or less representative of the several sections of the State, with greater percentages applying in centers of population concentration. Likewise, the distribution of infection as determined serologically is apparently rather evenly apportioned throughout the Commonwealth with, of course, higher percentages of positivity occurring in persons from the more densely populated section or communities.

These and an abundance of other data have been compiled relative to serological reactivity noted at the time of admission at the Prison as well as at the time of this survey, treatment and serological response thereto, etc., but it is entirely obvious that any appreciable expansion over the above figures and remarks would be impossible in such an elliptical summary as the foregoing. In conclusion, therefore, suffice it to say that, while the percentage of positive individuals at the South Carolina Penitentiary, as determined by the recent blood-testing survey, amounted to an average of 24.14% of the entire group,—8.09% of the whites and 36.53% of the negroes—and while those figures can probably be taken as constituting a fairly accurate index of the extent of syphilitic infection existing among inmates of this Institution, at the present time, it is the conscientious opinion of the writer that such figures can hardly be applied to the population of the state as a whole with any degree of accuracy, and especially as concerns the percentage of positivity for white persons (8.09%) which, while probably applicable in certain groups of low social and economic brackets, would appear somewhat excessive for the white population of the State as a whole.

PEE DEE SIXTH DISTRICT ASSOCIATION AND MARLBORO COUNTY MEDICAL SOCIETY HOLD JOINT MEETING

The Pee Dee Sixth District Medical Association and the Marlboro County Medical Society held a joint New Year's meeting, January 7, 1938 at Bennettsville, S. C. beginning at 3:30 P. M. From 3:30 to 5:30 P. M. an informal reception was held at the Marlboro County General Hospital.

At 5:30 the Societies and visiting physicians adjourned to the Masonic Temple where the scientific program and a dinner were enjoyed. The following papers were read.

Nutritional Heart Disease by Jos. I. Waring, Charleston, S. C.

Some Surgical Aspects of the Duodenum by Dr. Thos. D. Sparrow, Charlotte, N. C.

Influenza—Some Observations and Impressions by Dr. Wingate M. Johnson, Winston Salem, N. C.

Clinical Manifestations of Dysfunction of the Pituitary Gland by Dr. Robert Wilson, Jr., Charleston, S. C.

A motion picture was then shown entitled Complications of the Second Stage of Labor by Jos. B. DeLee.

After a three course turkey dinner talks were made by Dr. L. M. Stokes, President of the S. C. Medical Association, Walterboro, S. C. and Dr. Edgar A. Hines, Secretary S. C. Medical Association, Seneca, S. C. About one hundred and fifty doctors from this and neighboring states attended the meeting which was declared highly successful.

STUDIES RELATING TO THE CAUSES OF CANCER AND THERAPEUTIC APPLICATIONS BASED UPON THEM

From the Research Laboratory
of
The McLeod Infirmary
Florence, South Carolina

James C. McLeod, M. D., F. A. C. S.
and
Leonard J. Ravenel, M. D.

The studies that form the substance of this communication were undertaken from having become increasingly impressed, through clinical experiences and statistical accumulations, with the inadequacy of present methods of therapy to successfully cope with much of the pathology that is a part of malignant disease.

To qualify these views, we would point out that the measures in vogue embodied in the form of surgery and of the radiations, are, in a sense, local measures; bear no relation to etiology, and are definitely circumscribed in applicability. This is not said in disparagement of acknowledged virtues they possess.

So great is the multiplicity of angle and aspect of the material the basis of this article that in order to try to correlate various features in a summary comprehensive for the purpose and at the same time give expression to personal experiences and ideas it becomes expedient to offer a presentation designed in a manner somewhat apart from the conventional, of grouping data under separate and distinct captions.

To foster conciseness, details of analytical proceedures, description of methods, etc., are not placed in the text for the sake of brevity, but are available in entirety to those who may ethically desire them. Bibliographical references, if given, would form a list requiring almost as much space as the article itself, having been gathered from authoritative publications throughout the world. It is, however, the case that no allusions to specific points are made that do not find corroboration in the printed word, or in the records of our own experiments. All are likewise available, and citations will be gladly furnished upon request. By thus obtaining freedom from impedimenta we hope to become enabled to more clearly focus attention upon the main factors we believe characterize causes for the development of cancer; upon things that feature its actuality, and upon means of therapeusis based upon the understandings.

From having been able to convince ourselves beyond any reasonable doubt that it is possible to deleteriously influence cancerous growths and beneficially influence the symptoms attendant upon their presence by means of substances introduced in the body at points remote from the lesions themselves, there would seem to be less reason than ever for a hopeless attitude that this dreaded affection may not finally become susceptible of control.

Pathologists have, we understand, rather generally accepted the doctrine that cancer cells are cells that are permanently altered. They base this conception largely upon the demonstration that such cells may be propagated in artificial media through many generations, and upon being removed therefrom and transplanted into a suitable host, can again multiply and exhibit the features that originally characterized them. A definition or determination of the nature of the alterations, beyond subtle differentiations in morphology, has evolved upon other workers, and from their labors it is known that malignant cells exhibit quite marked differences in their metabolic processes

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as compared with normal ones. Regardless of whatever the cause or causes of cancer may be, there can be no question but that the manifestations are accompanied by very definite changes in the chemistry of the cells involved.

It may be held as certain, envisioning gross circumstances of living things, that growth cannot take place without acquisition by the organism, and its ultimate components, of those nutritive factors that comprise the essential elements of growth. Cells malignant exist side by side, as it were, with those that are normal, and it is incredulous to suppose that they do not, of necessity, derive sustenance from the same storehouse. But it is a proven matter that upon obtaining nutritive materials from the common source of supply, malignant cells carry these materials through paths of degradation that differ radically from those followed in normal metabolism. There is, furthermore, reason to believe that cancer cells are able to utilize food stuffs, or at least some of them, with less expenditure of effort than cells in normal balance are called upon to exhibit, and in so doing develop potentials that result in the excessive or uncontrolled proliferation at the expense of function that is an outstanding feature of malignancy.

Carbohydrates are looked upon as being the fundamental compounds that make up the fuel of life. From them proteins and fats are formed through synthetic combinations with other elements, and proteins and fats may in part be broken up to form sugars. These matters are extremely complicated, but it appears that in glucose, cells find a substance easily available for nutritive and other requirements, principally because the molecule, on account of its configuration, lends itself readily to chemical alterations with less energy requirement for the processes than is needed for the handling of food products of other nature. From this fact, and in consideration of the difficulties inherent in studies of the proteins and fats, the vast majority of biochemical research in cancer has had to do with mechanisms by which cells metabolize the sugars.

In utilizing carbohydrates, normal cells do so through the maintenance of an admirable balance between two basic chemical processes, fermentation and oxidation. By "fermentation" is meant a fission or fragmentation of molecules, and by "oxidation," an ultimate resolution of molecules into CO_2 and H_2O. Fermentation is much the simpler of the two, though far less economical, and undoubtedly preceded oxidation in the scale of life and evolution; the acquisition by Nature of the latter enabling development of the more complicated forms of living matter.

While it has been a teaching that cancer cells may be looked upon as cells that have reverted to an embryonal status, some exception may be taken to the statement, because embryonal cells are subject to restraint and become adult, thus assuming eventually the roles for which they were originally designed. Cancer cells do none of these things. There is, instead, much cause to consider them as cells that have reverted to a primitive or primordial status; one in which the reactions of oxidation have largely given way to elemental ones of a fermentative character.

It is common knowledge that one of the products of fermentation by yeasts is alcohol, and that in muscle and other animal cells, lactic acid is an intermediate product. It is of academic interest to realize that by empirical formula the difference between the two is merely that of a carboxyl group. In normal body cells, a series of reactions evolve about lactic acid and one of its immediate precursors, pyruvic acid, that eventuate in polymerizations and resyntheses upon the one hand, and in oxidations upon the other, so that the lactate is finally dispelled in one way or another. Not so in cancer, which not only forms lactic acid from glucose at a great rate, but, failing to use it properly, contributes the compound in quantity to the venous drains. In other words, there is a pronounced defect in the pyruvic-lactic cycle in the metabolism of malignant cells, concerned with inability to adequately burn or transform these, and perhaps other chemicals, as well.

To make comparisons more explicit in this regard, it is now accepted thought that glucose, upon being absorbed by normal cells, is first polymerized to glycogen. The glycogen then undergoes hydrolysis into hexoses that combine with phosphate. These in turn degrade into three carbon atom molecules, also in combination with phosphoric acid, and upon

interacting, eventually produce lactic acid. A considerable percentage of the lactic acid becomes reconverted to glycogen, whilst the remainder undergoes combustion. The combustion appears to be contingent, among other things, upon the development of a series of C4-di-carboxylic acids, commencing with oxaloacetic, that forms from pyruvic by carboxylation, and proceeding through malic, fumaric and succinic acids, eventually transferring hydrogen to a system of respiratory catalysts and enzymes that activate the oxidation-reduction systems and permit of the combustions in question. Students of biologic chemistry now express the belief that, beginning with the relatively simple process of carboxylation of pyruvic acid, Nature found means of proceeding from fermentation to oxidation. It therefore becomes of much more than casual significance, from the evidence that cancer shows reactions attending metabolism of the sugars that are mainly of a fermentative type at the expense of oxidative ones, that disturbances in the handling of pyruvate are demonstrable in connection with them.

At this point it is perhaps desirable to remark upon the possibility of the lactic acid formed in tumor being a racemic mixture, that is, a mixture of d- and l- forms. Only the l- form is capable of being resynthesized to glycogen; its isomer being resistant to the transformation or is only with great difficulty so changed. Perhaps the accumulation of lactate in tumor finds some explanation in a circumstance of this kind. To render the idea more striking, it has been found that if a normal dog be given an amount of l- lactic acid (which is the normally occurring form) and in a quantity computed to correspond to that given off in a space of time by a mass of cancer tissue weighing 600 grams, no lacticacidaemia develops, but the administration of a like amount of the d- type or isomer produced a decided increase in blood lactate. Coupled with reports in the literature upon the inability of the body to metabolize d- lactic acid with any degree of facility, much support is lent by the experiment to the hypothesis.

Not only does there appear to be a disturbance in cancer cells resulting in failure to properly utilize lactic acid after it is formed, but others that are notable. Cancer cells evidently imperfectly or incorrectly handle glycogen, both in point of formation and breakdown. Some tumors contain excessive amounts of this polysaccharide; others much less, when compared to the average normal cellular content. So little glycogen is contained in certain kinds of malignant tissues that the fact is made use of as a diagnostic test, as in the well known method of painting the cervix uteri with Lugol's solution. Glycogen is a colloid, and one of its principal functions appears to be to regulate osmotic pressures within the cell. Exerting of itself practically no force of this nature, it influences it tremendously by maintaining crystalloidal compounds in protoplasm at a fairly constant level by alternately splitting to produce them, and gathering them up by resynthesis. In tumor cells, glycogen has more of the characteristics of a static and stable compound, not at all labile in response to needs. To this is attributed the main reason for the upset in osmotic equilibria that evidence proclaims exists in malignant protoplasm. The reader is requested to bear this matter in mind in consequence of what is to follow, and with particular reference to microscopic pictures that present themselves of tumor cells that have been subjected to treatment.

Additionally, researches have directed attention to certain inabilities of cancer cells to properly carry out the phosphorylations and liberations of phosphate that normally accompany metabolism of the glucides. The matter is an extremely intricate one and about which the last word has not been said. It is conceded that glucose itself must first unite with phosphoric acid before becoming amenable of polymerization to glycogen, and there is considerable background for the supposition that, upon being taken up from the circulating fluids by malignant cells, instead of first becoming converted to glycogen, it undergoes decompositions. These decompositions are somewhat comparable to those that follow when the sugar is placed in mildly alkaline solutions. Among the resultant products occurs methyl glyoxal (pyruvic aldehyde), which, by taking up a molecule of water, may produce lactic acid directly. We would also especially call attention to the need of preliminary phosphorylation

of glucose for the normal enonomy, as the point is to be considered in connection with later ones in the discussion.

Those conversant with enzymic activities are well aware that the reaction of a medium can and usually does exert a profound influence upon the courses of reactions they inaugurate. Many people have reported upon changes in the pH values in malignant cells and in the fluids of the host. Our analyses in this direction, together with those of others, have shown a persistent shift in the reaction of the blood plasma of cancer patients toward the alkaline side. It may be that the accumulation of lactate in malignant cells and media promote the phenomenon, accountable for upon the basis that a combination of weak acid and strong base, such as sodium, affords a salt having an alkaline reaction in solution.

For several months, work in our laboratory was wholly taken up with studies attaching the monosaccharide, galactose. This sugar is considered to be but feebly utilized by normal adult cells. In experiments conducted we were able to show that, in vitro, cancer tissues apparently could affect the molecule with more ease than could normal muscle. This was a rather startling finding in that it has been shown that, to the extent galactose is utilized, it affords energies for growth far in excess of glucose, though the combustion equivalents of the two hexoses are approximately the same, and the gross chemical difference between the two exists in the relative position of an hydroxyl radicle. Young and rapidly growing cells are able to burn galactose with comparative facility. Perhaps it is to the ability of such cells to use it that much of their proliferative capacities are referable. The occurrance of galactose in breast milk as a component of the disaccharide lactose is relevant as a need is thus denoted for it in the economy of the developing infant, since Nature does nothing without purpose. Of still further interest is the fact that glycogen produced from galactose differs chemically from the glycogen evolving from polymerization of glucose, being, according to recent investigators, made up of a chain of 18 hexose units instead of 12 as is the usual animal starch. The possibility is to be considered that galactose may be produced in malignant protoplasm, arising from the split products of glucose through union, and from it a glycogen may form that is different chemically and in biologic behavior to the variety found in normal tissues. It may, moreover, prove to be the case that cancer cells can directly use any galactose that may be brought to them through the circulation.

Pyruvic acid is formed when lactic acid is dehydrogenated. Since there is evidence that it, like lactic, is in excess in tumor, and because there is evidence that it too is improperly utilized, it has been suggested that the increased synthesis of protein in cancer finds a commencement in the combining of pyruvate with ammonia to form alanine, an amino acid that is an important stone in protein building; and that also, from imperfect utilization of pyruvate because of incomplete degradation, increased synthesis of fats develop from acetic acid and its condensation products.

Controversies over various points of chemical aberrancies shown by cancer take up great space in appropriate periodicals, and new data is constantly being added. In mentioning briefly some of the things that are rather universally accepted, and in tracing the irregularities, one cannot not only fail to be impressed with the assumption of a fermentative type of metabolism by cancer over an oxidative one, but recognize that digressions from the normal are synonymous with equal disorder in the enzymic and catalytic functions responsible for the equations. Hence enzymic and catalytic dysfunction in a cell is entirely expressive of and parallels the disorder in its metabolism. Since and including the original contributions of Warburg respecting the respiratory quotients of tissues, numerous workers have confirmed the lessened degrees of oxygen consumption by tumors that are cancerous. Reports of this kind lend no little weight to the argument that the metabolism of malignancy is basically fermentative.

Pasteur found in working with yeasts, that if oxidation were diminished through lack of oxygen, fermentation began; and conversely, if oxidation were promoted, fermentation became suppressed.

Assuming that cancer exemplifies a state of cellular metabolism in which there is defective oxidation, the application of measures

designed to restore the defect might well be argued to have an influence in effecting a state of balance. In the abstract, this concept has constituted the scientific reason for the employment of the various solutions and chemicals used by ourselves therapeutically.

By processing certain non-pathogenic fungi for the purpose of extracting from them principles thought to be lacking in tumor cells, as later referred to somewhat in detail, and by injecting such principles parenterally in human cancer cases, we have been able to note surprising results. Solutions made from the mold, *Aspergillus niger*, and from the yeast *Saccharomyces cerevisiae*, have been principally employed, though *Rhizopus* and other varieties of fungi have received attention as sources of material.

Following upon suitable experiments designed to test possible toxicity of the extracts prepared, and carried out upon laboratory animals, approximately one hundred and fifty cases of advanced malignancy abandoned as hopeless have been given treatment in the rooms and wards of The McLeod Infirmary. Practically all of the patients treated evinced subjective improvement, and in many instances notable degrees of shrinkage of tumor masses took place. Where and when this shrinkage occurred, it was often readily demonstrable by actual measurement, and, location permitting, by photography to scale. The reductions in size took place with amazing rapidity; often a resolution of as much as thirty per cent by volume showing within twenty-four hours or less after the giving of the first injection. That changes were brought about microscopically commensurate with the gross ones was repeatedly determined by an expedient of performing biopsies upon isolated metastatic nodules of approximately the same size, duration and consistency, both before and at varying intervals after treatment, and noting the development of extreme grades of degeneration and even necroses. Such destructions were seen in subsequent sections to give way to fibroblastic invasions; succeeded by the usual reparations through hyalinization and scarring. Grossly, the microscopic events were recorded by the assumption of a very hard consistency and frequent lobulations due to the formation of strands of dense fibrous tissues traversing the tumors.

Accompanying the resolutions, pain was greatly relieved and sometimes entirely disappeared where previously it had been a constant and dominant symptom, requiring large doses of morphia for control.

It is desired to call especial attention that these happenings followed upon the initial injection, thus excluding the possibility of the reactions ensuing in the malignant tissues as being analogous to ones that have been commented upon in certain papers as a part of sensitization phenomena. To the contrary, with continued administration of the preparations, a degree of tolerance appeared to manifest and establish itself, with corresponding lessening of effect, and, in numerous instances with renewed activity by the growth, together with recurrance of subjective symptoms. This feature we have been inclined to attribute in a general way to the formation of specific immune substances functioning by neutralizing active principles. Further observations have afforded some promise of ability to partially overcome the obstacle by appropriate desensitization proceedures, and by permitting an interval of time to elapse between treatments, as any immunity developed seems to be short lived. The question, however, is by no means settled, and perhaps some mechanism other than or together with immunity is involved. We feel that it is easily possible that the substances actually responsible for the effects may not of themselves be antigenic, but, as given now, are perhaps bound to compounds that are, in which event the problem would be to conclude separations and discard the antigenic fractions.

No harmful effects have ever been noted following the treatments as administered; there has been complete absence of reactions approaching anaphylaxis and allied states. As a matter of fact, the injections which mainly were given intramuscularly, failed to evoke local response beyond a mild degree of soreness not much in excess of that naturally expected to accompany the mechanical introduction of any medicinal solution in equal volume by needle, nor systemic response beyond sometimes an elevation of body temperature a degree or two.

At no time have signs of digestion or liquefaction appeared at the sites of placement of the extracts. In the face of marked effects upon tumors occurring soon afterward, no other inference can be drawn but that of a specificity and ability possessed by the reagents to attack abnormal tissues in the form of cancerous growths, without exerting deleterious influences upon normal structures. It is important and suggestive to mention in this connection that in one case exhibiting a fibroid tumor of the uterus, and a cancer of the breast with regional and distant metastases, no changes became observable in the fibroid, although very decided degrees of resolution took place in the parent and secondary malignant lesions.

The foregoing paragraphs have dealt with matters that pertain chiefly to the chemistry of cancer, as representative of features through which malignant cells have come to be classed as "permanently altered" cells. The brief account is to be accepted in lieu of more detailed descriptions not only necessitating a separate article, but one apart from the present purpose. They have also dealt with what has repeatedly been seen to happen when substances calculated to effect restoration of these chemical abnormalities have been given parenterally. The gross and microscopic changes in tumor tissues following the treatments have shown that instead of a restoration of cellular equilibrium, as might have been predicted to happen from abstract reasonings, degenerations and destructions have been the outcome. From viewing the pathological sections, and comparing them in corrolary with changes in gross morphology, the conclusion is scarcely to be avoided that the primary effects of the extracts have been to cause a rapid dehydration of protoplasm, accounting for the sudden shrinkage of the masses. An extraction of fluids through the cell membranes would reasonably follow upon any quickly occurring reversal of osmotic pressures within them.

From what has been witnessed clinically, the impression has been gained that malignant tumors of different classes and varieties do not respond with equal facility; some being more susceptible than others, and some responding not at all. Growths exhibiting the greatest amounts of anaplasia have been affected the most readily, and in this grouping is to be placed cancers of the uterus and of the breast showing such characteristics, together with some types of rapidly developing sarcomata.

In the extracts used have been identified many enzymes and catalytic agents. Of the former, we have been particularly interested in certain oxydases and dehydrogenases; also with carboxylase which attacks alpha-keto acids such as pyruvic in the presence of the specific coenzyme that is the pyrophosphoric ester of vitamin B*i*. Regarding catalysts, we have isolated and utilized cytochrome, and the flavin complex with vitamine B*2*, together with the specific coenzymes that are necessary to complete this system of respiratory carrier. Both yeast and *Aspergillus* extracts contain catalase, whose action in the test tube is to liberate nascent oxygen from hydrogen peroxide, but whose function in vivo is considered to be concerned with liberating the gas from oxyhaemaglobin, and perhaps in assisting in transforming the liberated molecular oxygen to an active state.

It would be altogether impossible with the scope of this paper to discuss at any length the very complicated matters attaching oxidations in cells. The literature dealing with details of the subject is enormous. Suffice to say that the problem has of late become increasingly clear, in generalities at least, and the compounds that have been referred to as individual reactants are all very vital and essential links in the chain of reactions that normally ensue.

Upon factual analysis of what is exposed it will become apparent that yeasts and molds afford sources for the obtaining of the very principles, or many of them, that seem to be lacking in tumor substance, and upon whose presence oxidations depend. Hence there is little that can be classed as empirical in a therapeusis based upon the use of solutions prepared from these fungi, and which contain them.

Through relations in certain manners, other materials have been employed for similar purposes, and as instances we would refer to the extraction of lactic acid dehydrogenase from the heart muscle of the ox, and of catalase from

the liver of the cow, whence it has been prepared in crystalline form. We could also speak at some length of the influence of oxaloacetic and fumaric acids as hydrogen transporters and promoters of oxidations, and of their existence in certain extracts. Of equal importance also is the influence of the endocellular activities of the cells of the normal intestinal mucosa in forming many of the reagents alluded to as necessary for physiological activities, and this will be dwelt upon subsequently.

Through having attempted to describe some of the features that distinguish malignant cells and in so doing define conditions that cause them to exhibit alterations, no considerations have been given to any factors concerned with reasons why the transformations take place. To say that a cell has become "altered" implies that another status previously existed, and, in the case of cancer, the preexisting status is assumed to be a normal one, because the concensus of opinion is overwhelminly in favor of the supposition that cancer cells were at one time units functioning in entire accord with design and environment.

In speaking of the etiology of cancer, it is apropos to bring to attention some ideas that have found support and that have furnished applicability through our research, which, in our opinion, may well be intimately connected with and a part of the reasons why normal cells experience reversions that produce malignancy.

One celled forms of animals and plants obviously exist through properties inherent within themselves whereby they utilize food stuffs, functionate, and reproduce themselves. So do all living things, but in the multicelled structures that are our bodies there exists an interdependence between varied types of cells that, if lost, results in states of ill health or even exitus. Is it possible that cancer develops because of some loss or some upset connected with this vital relationship? By subscribing to the viewpoint there would be an essential agreement with ideas long held by able clinicians that a general disturbance precedes and accompanies true malignant disease. Yet granting this be so, cancer is not perforce the outcome. But by acting as a predisposing cause, exciting factors contributed by traumatisms of chemical or thermal nature, or in the form of direct violence, become active by precipitating the changes, long smoldering, that make for cancer in cells involved by them. Conversely, such traumatisms, in the absense of an underlying predisposing factor, are not alone sufficient to induce malignancy.

In criticism of this may be offered the comparative ease with which tumor growths can be caused to arise, as from repeated painting of the skin with tar derivatives and other substances. The so-called malignancies produced by artificial means cannot, however, be strictly compared because of numerous discrepancies with true metastatic malignancy, and this applies also in a measure to spontaneous tumors in rats and mice as have been the subject of intensive studies in attempts to correlate them with cancer in the human. Despite certain fundamental similarities between them, some distinctions should rightfully be acknowledged. Especially does this refer to details of chemical differences.

From time to time numerous theories have found expression that attempt to delineate or designate that which may be termed the systemic disorder prompting development of what cancer actually is. We shall not try to discuss those that have appeared, but instead endeavor to present our ideas of the matter and the reasons therefor.

No explanations that have been brought forth are quite complete in accounting for outstanding differences in behavior of so-called benign and malignant neoplasms, particularly as to why the former do not metastasize or seriously interfere with the host unless by assuming enormous proportions or otherwise influencing vital functions; and this in spite of the fact that benign tumors often possess growth rates in excess of malignant ones. Nor are clear proposals extant that denote why other neoplastic masses spoken of as "malignant" disseminate rapidly from the site of origin to produce secondary tumors referred to as "metastases." Recent expressions tend to regard benign tumors as representative of unusual forms of hypertrophies arising in response to stimulations largely of a hormonal nature. Taken in this light there is a constitutional basis for their development also, but doubtless one quite different from that which may well underlie cancer.

One can surmise whether the disseminations called "metastases" are invariably representations of a multiplication of cells that were at one time a part of the parent growth, transported from it by the circulation to distant and often bizarre locations, or if in actuality they may at times represent new and independent tumors originating in divers situations from cells of similar composition and character in response to a common stimulus or stimuli. While in the abstract this would accord with certain beliefs concerning embryonal rests, it is indeed contrary to accepted teaching, and the fact is that a spread of cancer very often and even commonly takes place via the circulations. But this may not always be the mechanism accountable for multiple tumors, and certainly nothing is known about cancer so concrete as to permit of absolute dogma.

Having become through our work and studies thoroughly impressed with the manifest disorders in the handling of carbohydrates by cancer cells, it was but natural to inquire into all known ways by which the animal organism utilizes these compounds. The part played in the digestion and absorption of the sugars and starches by the intestinal membranes, both physically and chemically, received much attention. It was only then that certain matters that hitherto had been recognized but disregarded assumed significance when taken into mind in connection with some pathological singularities. We refer specifically in this respect to the extraordinary immunity of the upper intestine to primary cancer, and founded upon this, the influence that intestinal dysfunction may have in causing cancer to develop.

The liver, pancreas and small intestine are not only directly involved in metabolizing sugars but are derived from a common embryonal anlage. Upon this account an inference could well be drawn that in order for certain functions to be properly performed a balance between their respective tasks is needful. The capacity of the liver to form glycogen and to effect other reactions has been known for many years. Likewise, properties of both internal and external secretions of the pancreas have been pretty thoroughly exposed, as have also those of the external secretions of the duodenum and jejunum. But until rather recently not much attention has been given to studies of physiological chemistry dealing with processes that attend absorption of digested substances from the lumen of the gut.

Now it happens that primary cancer of the pancreas is quite commonly met with, and primary cancer of the liver is by no means unknown, but careful analysis of pathologic data yields the information that primary cancer developing from previously intact glandular elements of the duodenal mucosa is so rare as to be a curiosity, if indeed it ever actually occurs. True, both carcinomata and sarcomata appear in the duodenum. The latter usually arise in the muscular and fibrous coats, and carcinomata or epitheliomata develop from cells a part of or lining the biliary or pancreatic ducts as they empty into the intestine. Still others originate from aberrant masses of cells constituting embryonal displacements.

Aside from the freedom from cancer arising from the glandular epithelium, the duodenal mucous membrane seems to possess a degree of resistance to malignant invasions by continuity, as witness the sharp delimitation of cancer of the pylorus to extend distally into the duodenal mucosa beyond a few millimeters. This is something that is constantly to be noted in the operating rooms. Where any extension greater than this occurs it passes behind the mucosa, forming an encircling infiltration and sparing the membrane itself. Moreover, cancer of the head of the pancreas seldom invades the duodenal tissues, though forming masses of tissue about it, sometimes producing obstruction from pressure, or ulceration from circulatory interferences.

In the older text books of physiology we read that the end products of digestion of the glucides are monosaccharides, which are passed through the intestinal walls to reach the portal circulation. It has now come to be recognized that while this is true, some very definite transformations take place in these simple sugars before being transmitted. With the possible exception of galactose (and the reader is asked to reflect upon what has been said of this carbohydrate in preceeding paragraphs), many physiologists now believe that monosaccharides undergo phosphorylation in being normally absorbed. They go further and state that

glycogen cannot be produced from unphosphorylated hexose. It also seems to be the case that for a hexose to unite with phosphate, it must first undergo alterations in its structural composition and be converted to an enolic form. So it is pretty generally conceded that the hexose molecule is primarily changed chemically, and is then combined with phosphoric acid to become an ester; both things being accomplished by the activities of the mucosal cells of the intestine during the absorptive processes.

Let us presume that some derangement interferes with the performance of these functions. In such event, unphosphorylated hexose would be delivered to the circulation and liver, which would experience difficulty in making glycogen out of it, and a series of disturbances would begin. Not only would the liver experience troubles, but also the tissue cells. No one knows in just what form glucose exists either in the portal or general circulations because of technical and analytical difficulties that now appear to be almost impossible to surmount, but there is indirect evidence that for the body cells to take up glucose and burn it through usual channels it must first become "activated" or changed from the structural aldose formula. By referring to the discussion of the chemistry of cancer it can be seen what may happen when cells are forced to utilize "unactivated" hexose.

A substance has been alluded to called "co-carboxylase," and identification made of it as the pyrophosphoric ester of vitamine B-*1*. Also mention that without it the enzyme carboxylase cannot attack pyruvic acid, which acid in normal metabolism is a forerunner of lactic. Co-carboxylase is now recognized as being an essential material for the proper combustion of carbohydrates. We desire to emphasize the significance of this and other analogous matter in relation to the duodenum.

The vitamines our bodies require are obtained from food materials. In natural sources, vitamine B-*1* exists as the di- or pyrophosphate (co-carboxylase), and also in a state comparable to the synthetic product that is without such union.

Upon being taken into the digestive tract, phosphorylated vitamine B-*1* experiences changes by which through partial hydrolysis the phosphate is either completely split off by acids, or by enzymes of the digestive juices (phoaphat-*ases*), or the co-carboxylase becomes resolved to the monophosphate which is inert in any capacity to activate carboxylase. During absorption, however, phosphate is reunited to hydrolyzed vitamine B-*1* through the activity of phosphat-*ese* enzymes in the mucosa, and in like way simple or synthetic vitamine B-*1* is converted to the ester.

That which concerns vitamine B-*1* in this regard is also probably applicable to compounds a part of the vitamine B-*2* complex, except that knowledge at present does not go much farther than to mark an essential function of this complex as one vitally concerned in carbohydrate metabolism, and that it is a component of the flavin respiratory system. Cozymase, a molecular aggregate connected with the system in question, and containing phosphoric acid in bond, is now considered to be a vitamine essential to life.

While it is thus not possible to write with authority about details attaching vitamine B-*2*, it is apparent that in whatever form vitamine B-*1* be ingested, in order to become active or remain active as co-enzyme it must be kept in union with phosphoric acid as pyrophosphate. These phosphorylations are clearly functions of the duodenal mucosa, and probably involve a number of vitamines and substances, aside from the B group, and simple sugars.

In consideration of these things, light begins to dawn. First, as to reasons why the duodenal tissues show such resistance to cancerous changes and invasions, and secondly, that the development of cancer in the body may be and we believe is directly related, not only to a lack of properly prepared hexose, but to a lack of active vitamine.

By no means have the physiological and chemical functions of the duodenum been completely elucidated. Other reactions of importance other than the ones mentioned are suspected as taking place, but concerning which there is as yet no direct proof.

The question will naturally be asked as to why the duodenal mucosa should remain resistant to cancer in the presence of an inability to properly perform phases of its work. The answer obviously is that physiological insufficiencies are rarely absolute; one seldom sees

an absolute insufficiency of insulin for example. Doubtless even in advanced incapacity, the intestinal cells retain enough property to effect transformations for their own needs without being able to carry out enough of them for the bodily requirement.

In recording our opinion that malfunction of the duodenum is the fundamental basis for the development of cancer in the human, explanations present themselves to account for matters that partake of clinical interest. That some malignancies proceed with extreme rapidity while others remain for years as comparatively innocuous tumors may be referable to quantitative degrees of duodenal insufficiency. Some answer can also be given to the matter of heredity in cancer through a transmission of tendency to specific disturbances in the duodenum, much as diabetes mellitus, dependent upon an insufficiency of insulin, manifests predilection for certain races and families.

We have accomplished a good deal in our laboratory in connection with studies surrounding some of the vitamines, as witness publications emanating therefrom. It has been the good fortune for it to have been the first to have accomplished synthesis of vitamine B-*1* ester (co-carboxylase) enzymically, which was done by a technic consisting essentially of incubating fresh duodenal mucosal scrapings obtained from the pig with synthetic vitamine B-*1* at a *p*H of approximately 6.8. Within late weeks the chemists responsible for the synthesis in point have found it possible to separate the ester formed from the mixture in a state of purity, and to effect quantitative conversion of B-*1* to the pyrophosphate.

While it seems extremely likely that a lack of co-carboxylase together with other compounds is very directly concerned in etiology of cancer, it by no means follows that the supplying of it and other substances to patients in whom the disease is established will cure their lesions. There is only the hope and belief that the administration of chemicals and compounds of this and related nature is the general route to solution of the problem. The correctness of this is to be adduced from facts presented which show that it is possible to profoundly and specifically influence certain kinds of cancer tissues by reagents introduced in the body at points far removed from the lesions themselves, and the accomplishment despite the employment of extracts that are incomplete in the present state of development and in point of conclusive knowledge of many things pertaining to them.

Extracts have been made from the duodenal mucosa of the pig in a manner as to be sterile and injectable; shown to contain, among other materials, the enzyme phosphat-*ese*. From using them clinically we have not witnessed changes in the pathology of tumor masses that often followed upon the giving of extracts of the fungi, but the patients receiving duodenal preparations alone have consistently reported themselves as feeling much better, which statements have been reflected in general appearances. Those cases that have been given treatment in the form of solutions obtained from yeasts, *Aspergillus,* and from the duodenal mucosa, together with certain catalytic agents, have done best.

In the process of evolving a treatment, and especially one so complicated and involved as is this, there is no way to gather statistical matter pointing to results in the absence of having decided upon a standard of treatment to begin with. It is obvious that essential and radical changes have been and continue to be made in means of processing raw materials, and in various technics, so that no such standard has been possible of adoption. Nor is it feasible to formulate statistics having much weight or value without a lapse of years. Many of the people we have endeavored to help were practically moribund when first seen, which would vitiate a statistical account. For these reasons there has been no consistent effort to accumulate such matter up to this time. Instead, our interest has been occupied with research in the laboratory and in bedside observations. As an outcome, we choose to present these conclusions:

(a) That cancer is a disease of metabolism.

(b) That we have proven to ourselves that it is possible for cancer to be attacked by substances given parenterally and reaching tumors by way of circulating fluids.

(c) That this happens without concomitant or subsequent harm to the host.

(d) That the materials used evolved from studies of causes of cancer, among which, as cause, evidence is brought forth to show that malfunction of the duodenum is a prime factor.

(e) That it is possible to almost invariably improve subjectively people hopelessly afflicted.

(f) That it is often possible to effect substantial degrees of resolution in cancer tissues, lasting for varying periods. While recurrances have been the rule, and these not showing response to treatment as followed in the beginning, there have been exceptional instances showing quiescence the eventual duration of which cannot be stated pending passage of time. Moreover, regarding resolutions, not a few have been observed of such extent as to be dramatic and unbelievable.

(g) That in no sense is any claim even remotely made or intimated a cure for cancer has been discovered. The present stage of development of the work offers much encouragement that this end may be attained through continued research.

(h) That it is our hope that others may interest themselves in pursuing similar approaches, and through expression of such interest means may be provided to enable the work, that has had a substantial beginning, to be carried on at the source, as well as in other places.

In terminating, we would remark that the people treated with the extracts, have, without exception, expressed gratitude for the help they obtained, and to reiterate that while it is wise to adopt an attitude of extreme conservatism and skepticism toward anything that is brought forth as a treatment for cancer, it is our feeling that the actualities presented are of such character as to constitute tremendous potentialities.

KERSHAW COUNTY MEDICAL SOCIETY

The following resolution was unanimously passed by the Kershaw County Medical Association on December 8, 1937.

Whereas, there is a great deal of discussion in the press as to State medicine and some prominent men have gone so far as to propose a bill in Congress which will place the control of the Practice of Medicine in the hands of a Bureau in Washington.

Resolved, that the Kershaw County Medical Association unanimously oppose any such action and insist that the present conditions be not interfered with politically.

Resolved, that this action of the Kershaw County Medical Association be published in the Secular and Medical papers.

At this meeting, the annual meeting, Dr. Brunson and Dr. Rhame were elected President and Vice-President and Dr. Humphries, Secretary and Treasurer.

An interesting paper on Coronary Occlusion was read by Dr. Stokes and Dr. Rhame discussed the dangers of and the removal of pimples about the mouth.

J. W. Corbett, M.D.
Corresponding Sec.

LANCASTER COUNTY MEDICAL SOCIETY

The Lancaster County Medical Society met at Lancaster, Saturday evening, December 4, at the home of Dr. R. L. Crawford. The topic for discussion at this meeting was the Lancaster County Hospital to be built in the near future.

The chief talk was made by Captain Elliott White Springs, who outlined with enthusiasm the help an up to date hospital would be to the physicians as well as the general public.

Only a few thousand dollars remained to be raised to insure the hospital. Fifty thousand was promised by the Duke foundation, 50,000 underwritten by interests of Captain Springs. All civic organizations have joined in the raising of the fund.

Those present at the meeting in addition to the doctors of Lancaster were Captain Springs, Senator Coke Bridges, Colonel R. S. Stewart, Mayor F. B. Porter, Dr. John Brewer and Dr. J. R. Turner of Kershaw, Dr. Buchanan of Winnsboro, Dr. Roy Steele of York and Dr. Roy Settle of Great Falls.

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FEBRUARY, 1938

DEATH OF DR. JULIUS H. TAYLOR

The passing of Dr. Taylor removes from the rolls of membership of the South Carolina Medical Association one of its most beloved members. Dr. Taylor very shortly after beginning active practice in Columbia manifested a serious and abiding interest in the affairs of organized medicine. He early became a member of the House of Delegates and served on numerous important committees often as Chairman. He played a significant part as Chairman of the Committee on Legislation in furthering the enactment of a satisfactory Medical Practice Law. In 1919 he was elected to membership on the State Board of Medical Examiners. In many other official capacities Dr. Taylor served the Association with distinguished ability. He was known throughout the state as a medical historian of deep learning. He rendered invaluable service to the Association and Woman's Auxiliary in their promotion of the erection of a monument on the State House grounds in Columbia to the memory of Dr. J. Marion Sims. Dr. Taylor received a crowning honor by being elected President of the South Carolina Medical Association. Owing to the state of his health he felt it incumbent for the best interests of the Association and for his own physical welfare to resign from this office in the summer of 1937. Dr. Taylor contributed largely to the scientific activities of the South Carolina Medical Association. He read many papers, chiefly on surgical subjects

The same enthusiastic devotion referred to above to organized medicine was displayed by Dr. Taylor in his membership in much larger organizations and this keen interest was rewarded by his being elected to numerous honorary positions. Dr. Taylor's genial personality won the hearts of medical men everywhere and they were delighted to honor him whenever opportunity offered. His presence will be keenly missed at our annual meetings and his enviable reputation will inspire the younger generation of physicians for a long time to come.

THE SPARTANBURG SOCIETY MOVES FORWARD

Under the guidance of Dr. P. M. Temples, President, and Dr. Ralph Mosteller, Secretary and Treasurer, the Spartanburg County Medical Society held one of its most enthusiastic meetings in recent years on January 24th. This Society has enjoyed a long and creditable career as one of the constituent societies of

the State Association having a membership of about sixty and with possibilities of some seventy-five members. The Society went on record at this meeting by increasing the County Society dues to ten dollars which includes the State Association dues. Guests of this meeting were Dr. Hugh Smith, Councilor of the Fourth District, Greenville, S. C., and the Secretary-Editor of the State Association. Plans are under way for enlarged programs and in increase of medical interest all along the line. Some of the most outstanding medical research in the world has been done in Spartanburg County and with such a background the growth of the Society interests is bound to be enhanced.

THE ALUMNI BUILDING CAMPAIGN

The Alumni Building Campaign is proceeding according to schedule and Mr. Brown has covered about one-half of the state. The large amount of time consumed in making personal contacts requires that this work be slow. Up to January 20th approximately $40,000 had been subscribed. This is a long way from being sufficient for a $250,000 building, but it is expected that there will be considerably more money subscribed and that a large part of the cost of the building may be obtained from State sources for the improvement of the Medical College.

J. I. W.

POLITICAL PLATFORMS

The need of more adequate funds for the Medical College and the natural consequent improvement in medical service to the people of the state are affairs of great familiarity to medical men. To find evidence that the situation at the college is becoming clear to the citizens of South Carolina and that the importance of the right sort of medical care is assuming its proper place in public consciousness is a matter of gratification and encouragement to the citizens who compose the medical profession.

The Charleston News and Courier of December 30, 1937, carries an account of an interview with Colonel Wyndham Manning, an announced candidate for governor, who said that "the farmer should have the same advantages of sanitation and preventive medicine enjoyed by the urban population."

"As a step in the direction of improved rural health, there should be provided a greater number of capable physicians and nurses in country areas," he said. "South Carolina, for the protection of her citizens, must give as liberal support to the Medical College of the State of South Carolina as the state can afford."

This is the kind of attitude in candidates for office that should be not only encouraged but also demanded by the medical voters of the state and all other voters, if they but realized it. Whatever Colonel Manning's ideas may be on other questions, the medical plank of his platform should definitely incline the profession and those whom the profession influences to support him. He has set a standard which will have to be met by other candidates for the governor's chair if they are to find equal favor in the eyes of the medical element of the state.

J. I. W.

EDISTO MEDICAL SOCIETY MEETING

Physicians from three counties, Bamberg, Calhoun and Orangeburg, comprising the membership of the Edisto Medical Society, heard an adress on "The Physician as a Citizen" by Dr. L. M. Stokes of Walterboro, President of the South Caroina Medical Association at a meeting in Orangeburg, Thursday afternoon, January 27 and elected officers to serve for the ensuing year.

Dr. C. I. Goodwin of Holly Hill was elected President; Dr. J. W. Harter of Orangeburg was elected Vice-President and Dr. H. M. Eargle of Orangeburg was reelected Secretary and Treasurer.

Delegates to the State Convention which meets in May are: Dr. J. W. Harter and Dr. G. C. Bolin from Orangeburg County; Dr. A. P. Traywick from Calhoun County and Dr. J. W. Lowman from Bamberg County.

SURGERY

WM. H. PRIOLEAU, M.D., F.A.C.S., CHARLESTON, S. C.

"THE IMMEDIATE TREATMENT OF INJURIES TO THE HAND"

The more general realization of the importance of early treatment of injuries to the hand would result in a great decrease of serious infections and permanent damage. In an article in Industrial Medicine (October 1937) Dr. Michael Mason considers this subject in some detail. He states: "If the open wound is seen within six hours after its infliction, the contaminants can be removed, the divided nerves and tendons sutured, and the skin closed with assurance that primary healing will occur." On the other hand, if treatment is administered after this favorable period, instead of cleansing and repairing the wound, the problem resolves itself into combating infection and secondary repair and closure. During the first few hours the organisms are adjusting themselves to their new enviroment and have not begun to invade tissues; thus they can be removed. After this period the tissues are infected, and the treatment has to be directed accordingly. Primary healing is not to be expected, and the suture of nerves and tendons must be postponed.

Most open wounds contain foreign material and devitalized tissue, both of which favor infection. Their removal is necessary before favorable healing can be expected. The open and contaminated wound is to be converted into a clean wound. Organisms, foreign material, and devitalized tissue must be removed. In so doing great care must be exercised not to inflict further damage. The delicate tissues must not be subjected to strong irritants, such as the commonly used antiseptics, for by so doing their power to combat infection will be decreased. As it is not possible to remove all organisms from the wound, it is important that the resistive powers of the tissues be not impaired.

A satisfactory technic is as follows: The surgeon scrubs as for any operative procedure and puts on rubber gloves. A piece of sterile gauze is placed over the wound, and the surrounding skin shaved and given a thorough cleansing with soap and water. Then with a fresh scrub see that the wound itself is thoroughly cleansed with soap and water, using gauze or cotton. Finally the wound is irrigated in all its parts with a quantity of normal saline solution.

The wound is then draped and a sphygmomanometer cuff applied as to tourniquet. A basin of sterile water is kept at hand for the frequent rinsing of the instruments. Devitalized tissue is carefully excised. In obtaining hemostasis small bits of tissue must be grasped in the forceps, and very fine ligature material used. To insure its being complete, the tourniquet must be released before the wound is closed. The divided ends of nerves and tendons must be accurately approximated and held in place with fine suture material, taking care not to injury them by grasping with crushing forceps, or ligating large bites. The gentle handling of tissue and proper hemostasis with a minimum of inert suture material are most important in obtaining a healing without infection. Wounds handled in this manner are better closed without drainage.

The author stresses the fact that tendon and nerve repair should be attempted only with adequate facilities and competent assistance. In the absence of these it is better that the wound be cleansed and closed, putting off the repair until it can be done under proper conditions. The application of an immobilization dressing or splint is an integral part of the immediate treatment of wounds of the hand.

DERMATOLOGY AND SYPHILOLOGY

J. R. ALLISON, M.D., COLUMBIA, S. C.

A BRIEF OF CUTANEOUS SYPHILIS

BY J. H .CROOKS, M. D., GREENVILLE, S. C.

Syphilis is a constitutional disease. The blood stream is early infested with the causative organism. The most characteristic manifestations are observed on the skin or mucous membranes, through which the infection enters the body. Therefore, the diagnosis of syphilis and its treatment are very important in dermatology as in medicine in general.

The terms primary, secondary, and tertiary, or early and late, as applied to different stages of syphilis are matters of personal opinion and are misleading at times.

The earliest clinical sign of syphilis is commonly the initial sclerosis or chancre, which appears at the site of inoculation. This is not always on the genitals but may be on any part of the body—lips, breasts, fingers, nose, or thighs, or wherever the contact takes place. The chancre is often accompanied and followed by regional and general adenitis. There may be malaise, anorexia, fever, headache, and other general symptoms. It must be borne in mind that a chancre does not occur in every case, or if it does occur, it may not be noticed by the patient or the examiner. The appearance of the chancre is varied according to location and type of tissue involved. It is usually round or oval, indurated, elevated, and crusted, the crust covering an ulceration. It is not at all uncommon to find more than one chancre on an individual.

The diagnosis of syphilis at the first appearance of the chancre is the most important decision the physician has to make. It may mean the difference between a cure and the failure to cure. In this early stage, we are now quite certain that by proper therapy syphilis can be cured. There is no excuse for the physician who begins antisyphilitic treatment in a patient who only presents a "sore" on the penis. Be absolutely sure that it is syphilis. No one can positively make a clinical diagnosis of syphilis by merely observing and palpating a penile lesion. If the darkfield is positive, the diagnosis is certain. However, if it is negative after a dozen or more examinations, one can only await a positive serology or the secondary skin manifestations,—the syphilitic rash—if it appears at all. But again, let me repeat, it is criminal on the part of a physician to give anti-syphilitic treatment until he is absolutely positive that he is really dealing with syphilis. Be positive. There is now no excuse for uncertainty. Depending upon the location, one must differentiate the chancre from a drug eruption, an injury, ulcerated herpes, chancroid, tubercular ulcer, epithelioma, Vincent's angina, lymphogran venereum, keloid, furuncle, abscess, granuloma pyogenicum, tonsillitis, simple ulcer, hemorrhoids, and apthous stomatitis. The history is important; the darkfield must be done if one is to be absolutely positive.

The syphilides or secondary skin manifestations of syphilis have an incubation period of 2—5 weeks to many months following the chancre.

The earliest of the skin eruptions is commonly the macular rash with universal or general distribution, including the palms, of a reddish to copperish color, progressive in development; tendency for lesions to become papular, accompanied often by general adenitis, mucous patches, moist and split papules in certain locations, alopecia, and in 95—98% of cases, a positive serology. The chancre may yet be present. The macular syphilide must be differentiated from drug eruption (especially that from copaiba), measles, the toxic erythemas, and pityriasis rosea.

The next most common skin manifestation, the papular syphilide, small and large varieties, appears at times with the macular type or occurs alone. It is usually early in the disease, and commonly universal or generalized. The papules may be limited to the palms, soles, face, wrists, genitals, and anal region, while other parts present the macular type. The papules of the commoner or larger type are of split-pea size and are not easily confused with other diseases. The moist papules are

only made so by their location, where there is heat, friction, and moisture, as the mouth, lips, and anal region. The large condylomalatum is also of this variety and is very contagious. The mucous patch or papule is often painless and overlooked and is to be differentiated from apthous ulcers, Vincent's angina, non-specific stomatitis and gingivitis, drug eruptions, lichen planus, lupus erythematosus, pemphigus (very rare), erythema multiforme, and leucoplakia. This can only be done by careful observation and the darkfield and serological examination.

The pustular eruption of syphilis appears most often in unhealthy and uncleanly persons. It is not a common type. There are usually three clinical varieties: the small or miliary; the large, acneform or varioliform; and the flat, impetigenous, pustular eruption. Pustular syphilide may be confused with smallpox, chicken pox, drug eruptions (especially iodide and bromide eruptions) impetigo, and ecthyma. The serology is most always positive at this time.

True vesicular or bullous eruptions due to syphilis are rare. Some doubt that such eruptions ever occur. Occasionally such cases are seen, the eruption being of a mixed type. When one sees an eruption composed of grouped vesicles, syphilis must be considered. Infants with congenital syphilis may present vesicles or bullae.

There is a discoid syphiloderm, the lesions being discrete, from a dime to a quarter in size, flat, raised above the skin level, and of the usual brownish red or copper color. In moist areas, the discoid lesions form condylomata. The face and trunk are favorite sites. It commonly occurs as a late manifestation of syphilis and in clinics is seen rather frequently. In the diagnosis, one must consider psoriasis, tuberculosis, drug eruptions, and other dermatoses. The serology is almost always positive.

Annular lesions of syphilis are most often seen in the negro, and according to MacKee are thought to be a relapsing or recurrent eruption, often preceded by a former syphilide of some other type It may appear during the latter part of the first year of infection, but more commonly during the second or third year The chin is the commonest site. Annular lichen planus, multiple ringworm, pityriasis rosea, granuloma annulare, and psoriasis may be confused with the annular syphiloderm.

From the second or third year until late in the disease, one may see squamous syphilide. Mixed types are common, the papulo-squamous, nodulo-squamous, the former being most common. The late lesions of syphilis seen on the palms and soles are often squamous and usually are unilateral and may be mistaken for psoriasis, eczema, and dermatophyosis, but lack the acute inflammation, the symmetry, and the border of the lesions are more irregular or gyrate.

The rupial eruption of syphilis is an ecrustaceous lesion, commonly about the size of a silver quarter, superficial and thickly crusted. The type occurs usually in individuals of poor general health and body hygiene.

The nodular syphiloderm is taken to be in reality a small, superficial gumma appearing as a rule, late in the disease, after the second year. The nodules range in size from that of a split pea, to a hazel nut. Every diagnostic test available may be necessary for a diagnosis. The nodular and ulcerated nodular lesion may be confused with epithelioma, tuberculosis, ioderma, bromoderma, and deep fungus eruptions.

The characteristic cutaneous lesion of tertiary or late syphilis is the gumma. It begins in the deep skin or subcutaneous tissue. It may appear the size of a walnut or an egg. It is attached to the skin and perhaps to other structures, the covering skin being of a copper red color. Ulceration is common, pain unusual. It may be single or multiple. The common sites are the legs and head, especially the nose, but it may occur in any part of the body. In so-called malignant syphilis gummata may appear in the first or second year. If between the third and tenth years, it is likely to be of the ulcero-nodular type. If after twenty or thirty years, it is common to see the single gumma or a few scattered gummata. Exceptions must be kept in mind. Differentiation must be made from the epithelioma, rhinophyma (rare), lupus vulgaris, erythema induratum (Bazin's Disease), tuberculosis proper, granuloma fungoides, drug eruptions (iodide and bromide, etc.), ecthyma.

The location, time of evolution, tendency to spontaneous involution, color, character of ulcer, tissue involved, scar characteristics, pigmentation, other evidences of cutaneous or visceral syphilis, and serology, if kept in mind will aid greatly in the diagnosis.

Some authorities speak of a chancre-redux. This type of lesion is thought to be a recurrence of a chancre within a few months, or it may signify a gumma that develops in the site of a long previous chancre.

Interstitial glossitis is a common and very interesting syphilitic lesion of the tongue consisting of extensive infiltration and fibrosis. Smooth atrophy and leucoplakia are commonly seen with this type. It responds very poorly, if at all, to the most intensive anti-syphilitic therapy. Cancer not infrequently develops on interstitial glossitis, and for this reason, the patient should be observed regularly from year to year.

Leucoplakia or leucokeratosis of the mouth is most frequently seen in syphilitic persons. It occurs most commonly on the tongue, the lips, and mucosa of the cheeks. Leucoplakia is not considered a true syphilide. The histopathology does not resemble that of syphilis. It responds poorly to therapy for syphilis, yet Rosen feels that syphilis is the cause of leucoplakia of the tongue in eighty-five percent of cases. Everyone is familiar with the milky white, pearly lesion of leucoplakia. The patient may be unaware of it. Its prototype is seen on the vulva in Kraurosis vulvae. When of syphilitic origin, it is a very late manifestation. Its chief danger lies in its common tendency to become cancerous. Arsenicals given for treatment of syphilitic leucoplakia has a tendency to hasten the formation of cancer. Treatment would best be confined to the heavy metals, especially bismuth. Vincent's angina, lichen planus, lupus erythematosus, mucous patches; apthous ulcers, mercurial stomatitis must be differentiated.

Alopecia of syphilitic origin is common in infants, but may be seen in any age. It differs entirely from other types of alopecia. The irregular loss of hair causes a peculiar moth-eaten appearance; the hair loss is not complete in any place. It is patchy and often configurate. It must not be confused with simple alopecia areata, tinea tonsurans, lupus erythematosus, morphea, lupus vulgaris, folliculitis declavans and pseudo-pelade.

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THE UROLOGICAL ASSOCIATION OF SOUTH CAROLINA

AN APPARATUS-METHOD FOR RESTORATION OF BLADDER CAPACITY

BY MARION H. WYMAN, COLUMBIA, S. C.

White female patient. Age 42. Has suffered with frequent urination for several years. Another physician had diagnosed Hunner's Elusive Ulcer of the bladder and had applied pure carbolic acid to the mucous membrane of the urinary bladder. At the end of about two weeks when the pain reaction had subsided, there developed moderate to severe hemorrhages from her bladder. The blood in her urine always appeared after patient had been asleep, probably due to an over-distension of the bladder. Rest in bed and all methods failed to control the bleeding, which continued for about five weeks before patient consented to

fulguration of the bladder. Under general anaesthesia, patient's bladder was fulgurated and forcibly distended up to about twelve ounces capacity. The next forty-eight hours, patient had no bleeding, but the capacity of the bladder remained small, the maximum being about four ounces. At this time, sixty grains of Sulfanilamide were given daily and a reverse decompression apparatus was attached to an indwelling soft rubber mushroom type of bladder catheter. At the commencement of the bladder dilatation patient's bladder only tolerated four ounces of fluid. A glass receptacle rubber tubing intravenous set was connected to the bladder catheter. The glass receptacle was elevated just a few inches above the patient's bladder or at the position the patient could tolerate in comfort. Sulfanilamide-ized urine was concentrated in the bladder, which was gradually distended by the kidneys secreting up to about twelve ounces. That amount, twelve ounces, was the extreme limit that the bladder would hold without discomfort. The Sulfanilamide-ized urine contents of the bottle was allowed to spill over when more urine than the twelve ounces entered the bladder. After a few hours, the patient was entirely comfortable and stated she actually did not know that the apparatus was in situ. After four days of continuous distension of the bladder up to this twelve ounces capacity, the treatment was discontinued. The dosage of Sulfanilamide was then reduced to forty grains per day.

During the past month since this distension treatment has been furnished patient's normal capacity is twelve ounces, and she is enjoying more comfort than she has experienced in several years. She gets up only once at night to void and is not inconvenienced by a frequent desire to go to the toilet during the day.

I wish to emphasize the gradual distension of the bladder by means of this apparatus and to restate that the bladder distension was accomplished with highly concentrated Sulfanilamide-ized urine. The Sulfanilamide was, of course, administered orally.

This method really accomplished remarkable results in this patient. These interstitial cystitis, fibrotic, small capacity bladders cause much suffering to patients and usually tax the urologists' ingenuity. I hope this method may help others and I shall appreciate hearing the results obtained by other physicians.

OBSTETRICS AND GYNECOLOGY

J. D. GUESS, M.D., GREENVILLE, S. C.

QUERIES AND ANSWERS

This month the editor will attempt to answer several questions that were asked during the obstetrical symposium held in Columbia in December. In passing, it should be observed that this meeting, initiated by Dr. Robert E. Seibels, Chairman of the State Committee on Maternal Welfare, but made possible by the hearty cooperation of the Columbia Hospital and the Columbia Medical Society, was an excellent meeting in every respect. About 100 doctors, each seriously interested in improving his understanding of obstetrical problems, registered. Dr. Ivan Proctor, professor of obstetrics and gynecology at Wake Forest College, discussed concisely the problem of prenatal care and showed a well executed motion picture illustrating the steps of such care. Dr. Lester A. Wilson, of Charleston, discussed the significance and treatment of abnormal findings in early pregnancy.

Dr. R. W. Ball showed the motion picture prepared under his supervision for public instruction with regard to the importance of prenatal care. This is an excellent picture, interesting and instructive, with nothing to offend even the most prudish, and it should be in great demand by the various county health officers for educational showings in their various counties. Dr. Holtzclaw, of Greenville, expects to show it in each of the four districts of his

county during January. The showing will be preceded by a short talk by a member of the State Committee on Maternal Welfare.

The following questions were among those asked during the round table conference, which closed the Columbia meeting.

Query: What effect, if any, does pregnancy have upon the reliability of the Wassermann test? X. Y. Z.

Answer: There is some difference of opinion in this matter. A negative Wassermann in the pregnant, or in the non-pregnant for that matter, is not necessarily significant. It may be caused by technical error. It occurs in many cases of latent and congenital syphilis, and in some syphilitics who have had inadequate treatment. On the other hand a strongly positive reaction, certainly in this country, indicates syphilis. Pregnancy seems at times to cause a negative reaction even in syphilis, and in doubtful cases it should be checked after provocative neoarsphenamine, and where there are strong clinical suggestions of syphilis, treatment is justified, even in the face of a continuously negative Wassermann reaction.

Query: What anodynes, or such, do you use or advise during labor? X. Y. Z.

Answer: The question of analgesia during labor is too big to discuss fully at this time. The selection is highly individualistic, depending upon whether or not the patient is attended by a competent nurse in a good hospital, the familiarity of the doctor with the method under consideration, the reaction of the patient to the method, and the difficulty of the labor as determined by position and presentation, and the relative demand for intelligent cooperation of the patient in the second stage of labor. This fact of selectivity is frequently disregarded in discussion of this subject, and yet it is highly important.

For the average man, attending the average case in the home without trained assistance, it is probably best to stick to morphine, morphine and atropine, or morphine combined with a small dose of scopolamine in the first stage, and intermittant chloroform or ether, in small amounts in the late second stage. One capsule of nembutal, or sodium amytal, or chloral hydrate quiets the nervous apprehension experienced by some women very early in labor without inducing the excitement that so frequently follows the administration of larger doses for analgesia later in labor.

Query: What anesthetic do you use in labor? X. Y. Z.

Answer: The answer to this question will depend upon whether or not the labor occurs in the hospital or in the home, also whether or not the delivery is spontaneous or instrumental. In the hospital in spontaneous deliveries, nitrous oxide gas and oxygen administered intermittently by a well trained anesthetist, is usually very satisfactory. The concentration of nitrous oxide in the mixture should not exceed 85 per cent. Higher concentrations may cause dangerous anoxemia in the baby.

Intermittent administration of ether may be safely used. Its pain-easing effect does not come on so quickly nor pass off so quickly as does that of nitrous oxide, and so it is not so satisfactory. Further, it tends to lengthen the intervals between pains.

Chloroform occupies a rather anomalous position. Theoretically, it is a highly dangerous drug, acting to paralyze the heart in the first stage of anesthesia—the stage employed in intermittent obstetrical administration—and to damage the liver if used for complete anesthesia. In spite of these theoretical objections many excellent and careful men continue to use it for intermittent administration in labor, and most of these have never recognized any ill effects from its use. It offers many advantages. It is not bulky, and so can be easily transported. It does not tend to deteriorate. It is effective in small amounts. It exerts its analgesic effects quickly and is as quickly dissipated. In fact, it can be used in a way similar to and about as satisfactorily as nitrous oxide—some say even more satisfactorily.

For deep anesthesia required in forceps operations, podalic versions and cesarean sections under general anesthesia, ether is safest and best and should be used.

Spinal anesthesia is said to have peculiar dangers when used for delivery by hysterotomy or otherwise. The writer has had no experience with intravenous or intrarectal anesthesia, other than rectal analgesia with ether in oil or a soluble barbiturate.

Then to answer the question asked, the writer uses nitrous oxide or chloroform for intermittent anesthesia or analgesia, and ether for surgical of prolonged anesthesia.

EYE, EAR, NOSE AND THROAT

J. F. TOWNSEND, M.D., F.A.C.S., CHARLESTON, S. C.

SURGICAL TREATMENT OF STRABISMUS

Dr. Maynard C. Wheeler, in the December, 1937, number of the Archives of Ophthalmology, page 1,000, gives a resume of the Surgical Treatment of Strabismus. From it the following is quoted except for Dr. Weeks's technique and the one item in the operative indications by Dunningham. Complete Tenotomy is apt to produce over correction, and it is not advised but "in treating divergence there is no danger."

Partial Tenotomy — Place suture in the muscle or tendon before performing tenotomy and secure it more or less firmly to either the stump or the overlying conjunctive. Usually the suture is tied tightly and left long for later adjustment.

Recession is the most popular operation on the ocular muscles today, used either alone or in conjunction with a shortening operation. There have been claims that recession weakens convergence even if Jameson's rule of not setting the insertion behind the equator is followed. Berens and Jameson believe that with greater experience with the recession operation one does fewer shortening operations. 1 mm. of recession will correct 5 degrees of deviation. 5 mm. recession of internal rectus muscle will correct 20-25 degrees and from 40-50 degrees by a bilateral recession.

Jameson favors one or two recessions for convergent strabismus and reserves the addition of an advancement operation for squint of very high degree or when operation is confined to one eye.

In Tucking the technique described by Speas is good. The objections are necrosis of the muscle, slipping of sutures, and an unsightly lump produced by the break in the muscle. The conclusions of its advocates is that it is ideal for phorias or very small trophias (up to 15 degrees).

Advancement—Some say that to advance beyond the stump is useless. Peter claims that 5-10 degrees more effect can be obtained by including the conjunctive, the capsule, and the muscle in the shortening process.

Objection to advancement:

1. Uselessness of the advanced portion.
2. Danger of scleral sutures.
3. Difficulty of placing such sutures securely.
4. Risk of torsion.
5. Unsightly thickening.

But many—Moore, Onfray, Saint-Martin, Woodruff, Peter—use advancement as primary operation in convergent strabismus, performing it on external rectus of each eye if necessary. 15 degrees is about average correction from one advancement. It is the more popular shortening operation today.

Resection—The Reese technique has served as the model from which individual variations have branched. Failure to get sufficient shortening is largely a matter of technique of not placing suture sufficiently far back in the muscle—unless one agrees with Peter's dictum that the resection should not extend beyond the tendon. Dr. Webb Weeks advises using the Reese technique with this change, that the double armed central sutures are placed from without inward, the fold of the suture being on the external surface of the muscle, the needles are carried through the tendon stump as in the Reese operation, but the muscle is brought forward by the muscle forceps and held in place over the stump of the tendon until the sutures are tied. In this way Dr. Weeks claims to get more degrees of correction as there will be less slipping of the sutures.

Age for Operation—Except for a "representative group of French oculists" who favor waiting until near puberty, the majority favor operating as soon as conservative methods of treatment have been given a trial and failed, regardless of age. "This means that many

children are ready for operation at 3 years of age or earlier." "Dunnington urged early operation to avoid secondary muscular changes, postoperative diplopia, and great physical and mental handicap;" and the development of permanent amblyopia in the squinting eye.

Anesthesia: in children, general anesthetic is best.

Sutures—Silk is still used by many but, "recent improvements in catgut sutures and particularly in the needles and the method of attaching them to the sutures have caused a number of surgeons to adopt such sutures for routine use. The great advantage of not having to remove the sutures has definitely outweighed the increased cost and the somewhat greater inconvenience in handling them. The sutures of 0000 ten day chromic catgut with atraumatic needles have been established as very satisfactory for work on the ocular muscles."

Conservative treatment consists of full correction of refractive errors as measured after cycloplegia has been induced, correction of amblyopia by various forms of occlusion, and stimulation of fusion.

Jameson, however, advises against postoperative exercises, at least not before firm union has had much time to become secure.

For the operative treatment of paralytic squint those interested had better read Dr. Wheeler's abstract.

PATHOLOGICAL CONFERENCE, MEDICAL COLLEGE OF THE STATE OF SOUTH CAROLINA

KENNETH M. LYNCH, M. D., PROFESSOR OF PATHOLOGY

Case of Dr. W. M. Rhett
ABSTRACT NO. 349 (43122)
November 4, 1937 (Founder's Day)

Student Gaillard (presenting abstract):

An 11-year-old negro boy, admitted October 11, died October 12.

History (from father): Well up to September 29th, when vomiting after meals was noted; later vomiting occurred more frequently and at irregular intervals, not related to meals. Vomitus had been yellow or white, but one day before admission a bloody color was noted in the vomitus. Vomiting said to be of projectile type. Nausea and hiccups have increased in severity since onset of vomiting. Drowsiness noted the day before admission, and became progressively more marked. No headaches. No convulsions. "Twitching of eye-balls" since day before admission to hospital. Qestionable history of diarrhoea, duration not stated. "Hasn't eaten for a week." No previous illnesses or symptoms.

Examination: Temp. 95.4, pulse 80, resp. 28, BP 142/90. A well-developed and nourished negro boy, apparently dehydrated, in semi comatose condition. Eyes twitching. Nose and mouth negative. Tonsils enlarged but not definitely inflamed. Posterior cervical lymph glands palpable. Pulsation in suprasternal notch. Chest: no abnormal findings. Heart: Apical impulse in 5th interspace 3" to left of mid-line. Heart slow and regular. No murmurs. Abdomen: soft. Liver palpated below umbilicus and felt to left of mid-line as well as to right; liver firm. Spleen not felt. No tenderness or other masses. Extremities: negative. Knee and biceps jerks equal and hyperactive; marked ankle clonus bilaterally; no Babinski or Kernig. Neck not stiff. Eye-grounds exam. (Dr. Townsend): negative.

Laboratory: No urine voided during 33 hours patient was in hospital. Blood (10-11): Hb 12 gms. (75%); WBC 39,950; polys 89% (71% filamented, 18% non-filamented), lymphs 8%, monos 2%, basos 1%. Blood and Spinal Fluid Kolmer and Kline negative. Spinal fluid clear, total cells 1 per cu. mm., globulin 1 plus, sugar 3 plus; culture negative; colloidal gold negative. Blood Chemistry: Urea N 165 mgs., Creatinin 12.4 mgs., sugar 125 mgs., cholesterol 150 mgs.; total serum proteins 9.14 gms., serum albumin 5.14 gms., serum globulin 4 gms.

Course: Temp. remained below normal for 12 hours, then rose to 100, and promptly fell to below normal where it remained. Pulse never above 92. Resp. 24 per minute for last 24 hours. 12 hours after admission BP 136/96. Bleeding from both nostrils noted about 18 hours after admission. Catheter passed, but no urine obtained in spite of 2000 cc. of glucose in Hartman's solution intravenously and subcutaneously. On morning of 10-12, breathing was Cheyne-Stokes type, BP 110/38. Vomiting some blood; stools tarry. Patient remained nearly comatose. Died on 10-12, 33 hours after admission.

Dr. Beach (conducting): Mr. Boggs, will you open the discussion?

Student Boggs: We have a history of nausea,

vomiting, and headache, and examination discloses a semi-comatose patient with muscular twitchings and a low temperature. These findings suggest urinary poisoning. The blood urea nitrogen is 165 mgs., bearing out the idea. This blood chemistry makes the case one of true uremia, not the symptomatic uremia syndrome that may occur with cerebral edema without actual nitrogenous retention. Anuria is also a striking symptom in this case. The three common causes of complete anuria are (1) bilateral obstruction of the ureters, (2) acute glomerulonephritis, and (3) poisoning.

There is nothing about the case to suggest bilateral obstruction of the ureters. There is no history of poisoning in the case. The particular poisons that could bring about anuria are turpentine, bichloride of mercury, and the new solvent (diethylene glycol) which has been used in this "elixir of sulphanilamide," which has caused so many fatalities in recent months. The suddenness of the onset of symptoms in one previously well is very suggestive of poisoning, but one can hardly make that diagnosis without the knowledge that something was taken.

There is nothing on the record to serve as a background for acute glomerulonephritis, but from the record as we have it, I believe that we must consider that explanation best. The kidney infection may have been preceded by a mild respiratory tract infection which escaped notice. The blood pressure is definitely elevated, and that tends to confirm the diagnosis of globerulonephritis. The blood cholesterol is normal, as one would expect in acute glomerulonephritis.

From the course of the patient while in the hospital, it would seem that there was a severe toxemia (as commonly occurs in acute nephritis), having its effect upon the myocardium so that cardiac failure occurred terminally.

I believe that the record shows urinary poisoning associated with anuria, but that is as far as we can go with what we have on the abstract. It may have been due to acute glomerulonephritis or to an exogneous poison.

Dr. Beach: Mr. Hutt, will you continue the discussion if you can add anything to what Mr. Boggs has said?

Student Hutt: I think that Mr. Boggs has discussed about all the features of the case. There is no question of anuria or of uremia. As Mr. Boggs has said, these could be due to either an exogenous poison or to glomerulonephritis. The only thing that I can see on the record to make me lean one way or the other is the very indefinite statement that the vomiting seemed to come on after eating. This point is not a definite feature of the vomiting in acute nephritis, and suggests that there may have been an acute gastritis, which, if present, would probably be a result of the action on the stomach mucosa of a poison.

Against this being acute glomerulonephritis, we have a child who was apparently perfectly well before the onset of symptoms of uremia. Furthermore the course is unusually rapid for nephritis.

The most likely thing seems to be an exogenous poison, such as bichloride of mercury or diethylene glycol, since both cause severe kidney damage.

Dr. Beach: The case is now open for general discussion by the staff and by our Founder's Day guests.

Dr. W. M. Rhett: I believe that no one has mentioned the enlargement of the liver. This suggests that not only the kidney was damaged (as proven by anuria and uremia) but also the liver. There was no evidence of congestive heart failure; so that cannot be given as an explanation for the enlargement of the liver. The combination of assumed liver damage with kidney damage makes the likelihood of poisoning much more definite, since the liver is not usually enlarged in other forms of kidney damage, especially other forms of acute effect on the kidney.

Dr. Beach: This case showed a number of unusual features, outstanding among which was the acute onset in a child previously healthy, with all the findings that go with uremia. Even more striking, from the clinical aspect, was the fact that at the same time there was another child with almost exactly similar history and findings on the ward, and that other child had also been perfectly healthy until the sudden onset of symptoms of uremia. The combination of circumstances made us feel very strongly that we were dealing with a poisoning, but we could get no history from either case of any drug treatment or other source of poisoning. The patients came from different parts of town and did not know each other. Somewhat later a third case of uremia with sudden onset appeared on the ward, and by that time we were sure of poisoning. Two of the patients were autopsied, but autopsy could not be obtained on the third.

Dr. Lynch: As Dr. Beach has mentioned, when this case came to autopsy we had some warning, from the clinical side, to expect something in the way of poisoning, although no history of poisoning could be obtained. The case presented here today was the second case autopsied; The previous case presented some features at autopsy that did not appear to be the usual acute glomerulonephritis.

When this case came to autopsy, we were looking especially for kidney changes, of course. There was some swelling of the cortex of the kidney, but not nearly as much change as we were expecting to see from the kidney findings during life. In addition to the swelling there were several small scattered infarcts, such as we commonly see from embolism, particularly in endocarditis. Since there was no obvious source for emboli in the case we were at a loss to explain the infarcts at the time of the autopsy.

In addition to these changes in the kidney, as you

can see here (demonstrating autopsy specimens). Dr. Wood thought that there was some necrosis about the central venules of the liver, but I was not very sure of that at the time.

Microscopically (using micro-projector) there was extensive damage to both the kidneys and the liver, far out of proportion to the gross picture. The whole system of secretory tubules in the kidneys are necrotic or severely degenerated. There is relatively little involvement of the glomeruli of the kidney, although in the region of the infarcts the glomeruli are also necrotic from vascular closure. In the liver there is also a very striking necrosis of cells, here the involvement being in the region of the central portion of the liver lobule, where all cells are remarkably affected, as you can easily see here.

Because of the suspicion of poisoning surrounding the cases we hurried the microscopic sections through and found that all of the cases thought to be of the same type clinically, were idenical histologically in the effect on kidney and liver. We asked the health department to begin a check on these cases.

At about this time in the story we heard of a negro man outside Roper Hospital, who was similiarly affected with uremia while in apparently good health. When he died, Dr. Peery was called to do the autopsy. In that case, the kidneys were distinctly enlarged, and the entire cortical zone was soft, yellow, and necrotic, as if the entire cortex of both kidneys had been submitted to infarction. This showed us, then, the significance of the small infarcts in the case under discussion today; they were the connecting link between tubular necrosis and complete vascular closure as seen in the adult not on the hospital service. Just how the vascular closure was brought about in these cases is by no means clear.

At this time we began to do some sleuthing on our own accord. The man who died outside the hospital was found to have taken some sulphanilamide. This drug has been much used recently, but no such effects had ever been observed to occur in patients so treated. At this time the newspaper story broke of the poisonings from an "elixir" of sulphanilamide. On that information we checked with the preparation of sulphanilamide which had been given the man, and found that it was the same "elixir." Subsequently all the patients in the group were shown to have been given a prescription, outside the hospital, for "Elixir Sulphanilamide," and the amounts given varied from two ounces to most of the children to six ounces given to one adult. We secured some of the material from the same bottle used for dispensing and had begun an analysis, when the nature of the poison was revealed in the lay press.

It was learned that the sulphanilamide, itself relatively harmless and a very effective therapeutic agent, had been mixed with diethylene glycol to render it soluble. This is strictly an industrial solvent, and has apparently never been used before in medicinal preparations. In the effort of the drug house to dissolve sulphanilamide (which is relatively insoluble in water, and is usually given in tablets or as a powder) they mixed the harmless drug with a dangerous poison. The effects are apparently due entirely to the solvent and not at all to the drug.

This case was presented here today because the group of cases has received much attention recently in the lay press, and also to allay the fears that some now have of using sulphanilamide in the usual, effective, harmless form. The drug stands cleared, but the solvent, diethylene glycol, stands convicted. Also open to great criticism is the drug house which would put out an untested preparation of any drug, and the physician who prescribes unproven drugs. It has been said that the practicing members of the profession are now taught therapeutics by the detail men of the various drug houses, rather than by scientific teachers and investigators. Such a catastrophe as the present group of cases serves to illustrate the dangers in such a method.

Dr. Beach: A funny thing about all the hospital cases was that the parents of all the children were questioned carefully about any medication they may have received, but that all denied that any medicine had been taken. Subsequently all were proven to have received the drug, as Dr. Lynch has pointed out.

Dr. Lynch: Yes, the case under direct consideration today received a prescription for four ounces of "Elixir Sulphanilamide" on October 2nd, was admitted to the hospital on October 11th, and died on October 12th.

Dr. Heyward Gibbes, Columbia: As I recall from this case, there was a gastro-enteritis present. Did the other cases show similar changes?

Dr. Lynch: No, they did not. This one case showed microscopic damage to the epithelium of the stomach, which, in view of the epithelial damage to kidney and liver cells, I thought was probably due directly to the poison; it may of course have been another manifestation of uremia, since such things are very common in uremia from ordinary causes. That is what you were getting at, wasn't it, Dr. Gibbes?

Dr. Regan: As Dr. Lynch has pointed out, the poisonous effects in these cases were not due to the drug, sulphanilamide, but to the solvent, diethylene glycol. Sulphanilamide is, of course, harmful in very large doses, but there is a wide range of therapeutic safety

Some harmful effects have been reported from the therapeutic use of the drug sulphanilamide in its usual form—notably fever, sulphemoglobinemia and methemaglobinemia, but these clear up readily when the drug is discontinued. The cyanosis frequently observed during the use of the drug is apparently not harmful, if actual changes in the blood do not occur.

Some have suggested that the taking of magnesium sulphate in association with sulphanilamide makes sulphemoglobinemia or methemoglobinemia more apt to occur. Skin rashes and hemolytic anemias have been observed to follow the use of the drug therapeutically in rare cases, but the mechanism of their production is not clear, and even these effects clear up under proper therapy without bad effects, in most cases.

Dr. J. T. Quattlebaum, Columbia: Is there any indication that there is danger in using sulphanilamide in patients whose kidneys are already damaged?

Dr. Regan: Since the drug is eliminated largely in the urine, in cases of kidney damage the drug is probably not eliminated so readily and the therapeutic level in the blood (about 10 mgm. per hundred cc. of blood) is therefore reached earlier in these cases. Hence in cases with known kidney damage the drug should be used in smaller doses, and the level of the drug in the blood carefully watched.

NEWS ITEMS

ANNOUNCEMENT

The Southeastern Surgical Congress will hold its Ninth Annual Assembly in Louisville, Kentucky, March 7, 8 and 9, 1938, at the Brown Hotel. Thirty speakers from various States in the United States will appear on the program. South Carolina is honored by having the following places on the program. Dr. Austin T. Moore of Columbia will read a paper on The Treatment of Fractures of the Hip Joint by Extra Articular Fixation with Adjustable Nails and Dr. James McLeod of Florence on Non Penetrating Wounds of the Abdomen. Completed programs will be mailed out between 15th of February and the first of March. This is said to be the most extensive post graduate surgical assembly held anywhere in the nation. For information write to Dr. B. T. Beasley, Secretary-Treasurer, 701 Hurt Bldg., Atlanta, Georgia.

The wedding of Miss Sue Stevenson and Dr. Isaac Hayne, Son of Dr. James A. Hayne, State Health Officer, took place February 8 in the Methodist church, Denmark, S. C. The ceremony was attended by the immediate families of Miss Stevenson and Dr. Hayne. The bride is the attractive daughter of Mr. and Mrs. Stevenson of Denmark. For the past few years Miss Stevenson has made her home in Columbia, where she was graduated from the Columbia Hospital. Dr. Hayne was graduated from the South Carolina Medical College in Charleston. Dr. and Mrs Hayne will reside at Congaree where Dr. Hayne practices his profession.

Dr. Irving S. Barksdale, Commissioner of City Health Department, Greenville, S. C. addressed the American Business Club at the Woodside Grill, Tuesday night, February 1. Dr. Barksdale spoke on the living conditions found in the city today in comparison to those of several years ago. He said that modern medical science has made the city comparatively immune from epidemics. One of the largest crowds of the year was present for the meeting.

Dr. and Mrs. D. Lesesne Smith, Jr., of Spartanburg are being congratulated on the arrival of a son born, January 14. He has been given the name, Daniel Lesesne Smith, III.

Dr. P. J. Boatwright and Mrs. Boatwright, natives of Darlington, now residing in Orangeburg, announce the arrival of a daughter. Mrs. Boatwright is the former Miss Ann Ware of Darlington.

An address by Dr. Thomas Brockman, President of the Greenville County Medical Society and screening of a United States Public Health service film were the major attraction at a community mass meeting, February 9, in an educational drive on syphilis held in the South Main Street Municipal Hall, Greenville, S. C. The Junior Chamber of Commerce sponsored this first county wide campaign against the disease which kills 100,000 Americans annually. More than 200 community leaders in the fields of religion, medicine, education and civic and professional endeavors received invitations in addition to other adults.

Dr. Harper came to Anderson four years ago entering the profession of medicine with his uncles, Dr. J. R. Young and Dr. Henry Young. Dr. Harper is a graduate of Davidson College, of the Medical College of Vanderbilt University and of the University of Louisville.

Mr. and Mrs. D. S. Vandiver of Anderson announce the engagement of their daughter, Sara and Dr. Henry Young Harper, the wedding to take place February 19. On Friday, January 14, this interesting announcement was made known to a number of Miss Vandiver's friends, when Mrs. Vandiver entertained with a lovely contract bridge party. Miss Vandiver is a native of Anderson and a graduate of Converse College, Spartanburg, S. C.

SOCIETY REPORTS

LAURENS COUNTY MEDICAL SOCIETY

The regular meeting of the Laurens County Medical Association was held January 31st at the new Hospital in Laurens at 7 P. M. A three course dinner was served by the Hospital management which was thoroughly enjoyed by the large number present.

New officers for 1938 were elected as follows: Dr. F. K. Shealy, President, Clinton; Dr. M. B. Nickles, Vice President, Laurens; Dr. J. L. Fennel, Secretary-Treasurer, Waterloo. Dr. Martin Teague of Laurens was elected delegate to the State Medical Association with Dr. Rhame of Clinton as Alternate.

Three new members, Dr. B. H. Henry, of Clinton, Dr. F. L. Webb of Clinton and Dr. W. T. Martin of Goldville were received into the Society.

The new President, Dr. Shealy, was escorted to the chair and in a happy little speech urged all members to attend the meetings and do their full duty to the Society during the coming year. The next meeting will be held at Clinton February 28.

J. L. Fennel, M. D., Sec.

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OTOLARYNGOLOGY—Two Weeks Intensive Course starting April 4, 1938.

OPHTHALMOLOGY—Two Weeks Intensive Course starting April 18, 1938; Personal Course in Refraction.

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